SIGMA XI QUARTERLY

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SEMI-CENTENNIAL, ITHACA, JUNE, 1936

IN THIS ISSUE

CIRCULATION THIS ISSUE OVER 12,500

IN DECEMBER ISSUE

BAKER ON RURAL YOUTH
BRAMBLE ON FORESTRY AND CCC
DOHERTY ON ENGINEERING EDUCATION
BUCHANAN ON PROBLEM OF THREE BODIES
JACKSON ON EDUCATIONAL ADVENTURE

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SIGMA XI QUARTERLY

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THE SEMI-CENTENNIAL

This important event in the history of our great society and of the promotion of research in the United States and Canada is scheduled to take place in Ithaca, New York, June 19 and 20. The American Association for the advancement of science is generously cooperating with our committee of arrangements and has made our semi-centennial program a part of the plan for the summer meeting of the Association which will convene in Rochester during that week.

The Sigma Xi program will be a brilliant one. An English scientist of international renown is considering our invitation to give one of the principal addresses of our celebration—namely that on Scientific Research and the Social Order, Present and Future. The president of one of our best-known technical institutions has been invited to give the address on "The Service of Sigma Xi in the Universities of the Future."

Dr. Willis Rodney Whitney, until recently director of the famous research laboratory of the General Electric Company and now Vice-President of the company in charge of research, will speak on "The Accomplishments and the Future of the Physical Sciences." While Doctor Whitney has been one of the prominent scientists of this country in his able pursuit of research in applied science, he has never lost sight of the enormous value of investigations in pure science and because of his enthusiastic interest and extraordinary ability the General Electric Company has generously supported research in scientific theory.

Prof. Frank R. Lillie, the widely-known professor of embryology at the University of Chicago will represent the biological sciences on the semi-centennial program, speaking on "The Accomplishments and the Future of the Biological Sciences."

The Trustees of Cornell University have voted to erect a bronze tablet on the campus commemorating the Semi-centennial of Sigma Xi and have engaged an architect to design the tablet and an art firm to make it.

Early in October after chapters and clubs have resumed activities for the academic year their representatives on the Semi-centennial Committee will be asked to secure nominations for the Semi-Centennial Research Prize. There are to be two of these of $1,000 each—one for a worker in the physical sciences and one for a worker in the biological sciences. Chapters and Clubs are requested to name one candidate for each of these awards. The nominations are to be made to the office of the national secretary before February, 1936, and the awards will be decided by a committee especially appointed by the national president as follows:

Prof. Harold C. Urey, Columbia University, chairman.
Dean Joseph W. Barker, Columbia University.
Prof. George A. Baitsell, Yale University.
Dr. William B. Castle, Harvard Medical School.
Prof. Edward U. Condon, Princeton University.

Since last April work has been in progress in the office of the national secretary on the proposed Semi-centennial History and Record to be issued as part of our celebration. We have on our records upwards of 27,000 names of Sigma Xi members and associates. The labor of bringing the addresses up to date is prodigious with our limited staff of office assistance. Alumni Recorders of the institutions where there are chapters and clubs are cooperating with us to the extent of their information. The volume will give a complete list of members and associates, with their last-known address, their field of work, their professional specialty and their avocation or hobby.

The program of the celebration:

Friday Afternoon, June 19

a. Greetings from Cornell University.

b. Response from the President of Sigma Xi.

c. A brief history of Sigma Xi.

d. Address: The Service of Sigma Xi in the Universities of the Future.

Friday Evening, June 19

a. The Semi-centennial Dinner.

b. Address: Scientific Research and the Social Order, Present and Future.

Saturday Morning, June 20

a. Unveiling the Semi-centennial Memorial Tablet.

b. Address: Accomplishments and the Future of the Physical Sciences. Dr. Willis R. Whitney, Vice-President of the General Electric Company, in charge of Research.

c. Address: Accomplishments and the Future of the Biological Sciences. Prof. Frank R. Lillie, University of Chicago.

FOUNDERS OF SIGMA XI AND THE SEMI-CENTENNIAL

The founders of Sigma Xi and charter members of the Cornell Chapter were:

William Asher Day, Cornell '86, Frank Van Vleck, Stevens Institute of Technology '84, who when the society was organized was the youngest member of the Cornell University Faculty.

William H. Riley, Cornell '86, Harry E. Smith, Cornell '86, who after graduation became a professor of mechanical engineering at Texas Agricultural College.

William A. Mosscrop, Cornell '86, who later became engineer of supplies of the New York Telephone Company.

Charles B. Wing, Cornell '86, who was elected as a graduate student member of the chapter and who became professor of engineering at Leland Stanford and was a chapter member of the Stanford Chapter.

John Knickerbacker, Rensselaer Polytechnic Institute '86, who at the time of election to the chapter was a graduate student and afterward founded and was president of the Eddy Valve Company.

John J. Berger, Rensselaer Polytechnic Institute '86, also a graduate student at Cornell when Sigma Xi was started, and who died early in his career.

Edwin N. Sanderson, Rensselaer Polytechnic Institute '86, likewise among the graduate students at Cornell, who has been a successful engineer and contractor in New York City.

Prof. Henry Shaler Williams, who at the time of the actual organization of Sigma Xi was professor of geology at Cornell, who in 1886 had already formed a society of geological students but who saw the need of a society of broader scope.

Of those founders and charter members the national secretary has definite information to date that six are still living: Messrs. Day, VanVleck, Riley, Mosscrop, Wing and Knickerbacker.

It is proposed to have all living founders present at the Semicentennial as honorary guests.

THE GOVERNMENT'S RESPONSIBILITIES IN SCIENCE*

KARL T. COMPTON

President, Massachusetts Institute of Technology

The range of opportunity in science in this country is so great and the extent to which the government should undertake responsibility in this field involves such complex considerations, that it is perhaps rash to undertake a discussion of the problem. Nevertheless, the problem is as important as it is complex and events of the last two years have conspired to focus on it the attention of several organized groups of scientists with the result that some aspects at least of the problem have been somewhat clarified. I will attempt, therefore, to give a brief sketch of the problem of the government's present responsibilities in science, together with some suggestions as to ways in which these responsibilities may profitably be extended as they have been developed through discussions in the Science Advisory Board and in conferences with many other agencies and individuals.

My own contact with this study dated from a radiogram from my assistant, received in the summer of 1933 while on the boat from Boston to Bangor, stating: "Word received that you have been appointed chairman of committee to re-organize Federal Government." Realizing that there was some major misunderstanding, I was naturally interested to learn what had really happened and found in the paper on the following day that the President had appointed a Science Advisory Board of scientists and engineers with authority "to appoint committees to deal with specific problems in the various departments."

This Board now consists of fifteen men, including: Doctor Campbell, president, National Academy of Sciences; Doctor Bowman, chairman, National Research Council; Doctor Dunn, president, J. G. White Engineering Corporation; Doctor Jewett, president, Bell Telephone Laboratories; Doctor Kettering, president, General Motors Research Corporation; Doctor Leith, professor of geology, University of Wisconsin; Doctor Merriam, president, Carnegie Institute of Washington; Doctor Millikan, director, Norman Bridge Laboratory of Physics, California Institute of Technology; Doctor Adams, professor of organic chemistry and president of the American Chemical Society; Doctor Flexner, director, Rockefeller Institute for Medical Research; Doctor Jones, professor of plant pathology, University of Wisconsin; Doctor Lillie, dean of the Division of the Biological Sciences, University of Chicago; Doctor Rosenau, professor of preventive medicine and hygiene of the Harvard Medical School and professor of epidemiology at the Harvard School of Public Health; Doctor Parran, state commissioner of health of New York.

I discuss the work of this Science Advisory Board with some hesitation on two grounds. In the first place, your distinguished president, Doctor Angell, is reported in the press to have raised a question as to whether the services to

* Address at Sigma Xi initiation, Yale University. Printed by permission of Doctor Compton and of Science Press.

government by members of educational institutions may not sometimes be of less public value than their regular services in their institutions. You have probably heard the remark attributed to Pres. Nicholas Murray Butler in commenting on the large exodus of Columbia University professors to government posts: "Columbia's loss is the nation's loss." In the second place, there are those who feel that the efforts of well-meaning experts to assist the country through their services to the government in these times of distress, have not all been well considered or successful. Some of them are unfortunately analogous to the attempt to relieve the darky who had swallowed a potato bug by administering to him a large dose of Paris green to kill the potato bug.

However these things may be, the Science Advisory Board has found certain directions of usefulness in a modest way, and through its consideration of problems of the scientific services of the government has formulated the broad outlines of a plan whereby the scientific forces of the country may be strengthened and put to work more effectively for the national welfare. Before discussing this plan it will be helpful first to see where the government now fits into the picture of scientific activities of the country.

The scientific services of the government are spread through forty federal bureaus, of which eighteen can be called primarily scientific. Although their operations involve only about half of 1 percent of the federal budget, their work is absolutely essential to the national welfare in agriculture, manufacture, commerce, health and safety.

Typical problems in the administration of these bureaus are: Is the organization adapted to the best fulfillment of its objectives? Are its objectives of distinct importance for the public welfare? Is its program planned with vision and keen appreciation of needs and opportunities? Are old projects dropped when their objectives have been attained? Is the personnel competent and alert? Is there proper coordination and cooperation with non-governmental agencies? Are the most up-to-date methods in use? Is there unwise duplication of effort? Should a given project be handled by a governmental bureau or left to non-governmental agencies? What is the best expert advice on a given problem of public interest?

Problems like these are always present and require constant attention if the government's scientific work is to be maintained on a plane of high efficiency. Disinterested and competent advice is desired on occasions by the secretaries of departments, and similar advice and help are useful to the chiefs of bureaus.

The following three steps have been taken by the Federal Government to provide for itself disinterested and competent advice upon scientific matters:

(1) The National Academy of Sciences was established by an Act of Incorporation "enacted by the Senate and House of Representatives of the United States of America in Congress assembled," and approved by President Lincoln on March 3, 1863, said act specifying that "The Academy shall, whenever called upon by any department of the government, investigate, examine, experiment and report upon any subject of science or art, the actual expense of such investigations, examinations, experiments and reports to be paid from appropriations which may be made for the purpose," subject to the condition that "the Academy shall

receive no compensation whatever for any service to the Government of the United States."

(2) The National Research Council was organized in 1916, at the request of President Wilson, by the National Academy of Sciences under its congressional charter, as a measure of national preparedness, and perpetuated by the National Academy of Sciences on April 29, 1919, at the President's further request, as expressed in Executive Order No. 2859. The National Research Council is, in a sense, an operating arm of the National Academy of Sciences and is permanently organized into divisions, with representatives from all major scientific bodies, to further the interests of science and technology within and without the government.

(3) The Science Advisory Board was created by President Roosevelt by Executive Order 6238, July 31, 1933 (supplemented by Executive Order No. 6725, May 28, 1934), "with authority, acting through the machinery and under the jurisdiction of the National Academy of Sciences and the National Research Council, to appoint committees to deal with specific problems in the various departments," with terms of appointment to expire July 31, 1935.

The appropriations for the scientific bureaus of the government have been greatly reduced since the affluent days just preceding the depression, by amounts ranging in some bureaus as high as 60 percent. According to Mr. Ralph Ward the 1935 budget shows the following appropriations for scientific work:

10 bureaus in the Department of Agriculture	$38,276,000
5 bureaus in the Department of Commerce	11,522,000
2 bureaus in the Department of Interior	1,232,000
8 bureaus in the Navy Department	3,918,000
1 bureau in the Treasury Department	9,313,000
6 bureaus in the War Department	4,503,000
National Advisory Committee for Aeronautics	1,453,000
Smithsonian Institution	864,000

These figures include only expenditures for scientific work, except in the Department of Agriculture, where they include all appropriations to the bureaus, since it is difficult there to separate the scientific work from other activities.

Taking all of these appropriations into account it is found that only about .3 of 1 percent of the total budget of the Federal Government goes into scientific work. In comparison with the importance of scientific work to the country, this is certainly not a large proportion. One might well raise the question as to whether an increase in this amount might not bring advantages to the country which are large in comparison with those resulting from many of the other far larger expenditures.

It is interesting to consider these expenditures against the total background of expenditures for scientific work in the country from all sources. Mr. Watson Davis, editor of *Science Service,* has estimated the total national expenditure for work in science by government, industry, foundations and universities to be somewhat less than $100,000,000 per year. It is seen, therefore, that the

Federal Government accounts for roughly half of the total national expenditure for science.

It is also interesting to consider the part played by the universities from the standpoint of expenditures for science. The United States Office of Education Pamphlet No. 58 gives the following statistics for the academic year 1934-1935: 81 publicly controlled universities and colleges, with a total budget of $81,774,000 reported $9,526,000 as appropriated for research work. The major portion of these appropriations were for agriculture. Of the 81 institutions here listed only 47 reported any appropriations for research. Of 219 privately controlled educational institutions with aggregate budgets of $57,600,000, practically all of the research funds were reported by 16 of these institutions, and their aggregate expenditures for research were $1,627,000. It is evident from these figures that, important as research in educational institutions may be in developing new knowledge, their total expenditures for research are very much less than are the expenditures of the Federal Government for scientific work. It must be remembered of course that most of the government's expenditures for scientific work are not for research but rather for the accumulation of scientific and technical data, or the administration of technical services.

It is of interest to note the part played by the philanthropic foundations in this whole program. Doctor Keppel, in an address at Brown University last year, stated that in 1931 the philanthropic foundations of the country distributed $54,000,000, of which about $10,000,000 were for encouragement of research, exclusive of the very important fields of medicine and public health. Taking two of the largest of these foundations as examples, we note that the Carnegie Corporation in 1933 made grants of $68,000 for scientific research in the United States and its scientific agency, the Carnegie Institution of Washington, reported total expenses of $1,576,000. Similarly the Rockefeller Foundation in 1933, out of total appropriations and expenditures of $14,754,000, made appropriations of $4,509,000 for the natural and medical sciences and public health.

It is of course extremely difficult to justify the accuracy of these figures because of the differences in manner of reporting, but certain general conclusions can safely be drawn. The Federal Government is by a very large margin the largest scientific agency in the country. The next largest single unit consists of the agricultural work of the Land Grant colleges and universities. Excluding these the aggregate expenditures for scientific research by the universities of the country are comparable with the expenditures of the philanthropic foundations for these purposes. (As stated above, these conclusions are necessarily very rough. A major uncertainty lies in the definition of scientific work. If the expenditures of universities for educational work in science had been included, their position would of course appear much more prominently in the financial comparison.)

With this general background showing the distribution of scientific work in the country, let me now turn to a description of some typical problems of the federal scientific services which have engaged the attention of the Science Advisory Board and its committees during the past two years.

The first problem submitted to the Board was a request by the Secretary of Agriculture for a study of the United States Weather Bureau and recom-

mendations for improving its service. There had long been recognition of economic and other advantages which would result if the accuracy of weather forecasting and of other meteorological data could be improved. The issue may have been forced by a critical survey and report of the Weather Bureau by a committee of the American Society of Civil Engineers and by the disaster to the airship Akron. The Board's study of the Weather Bureau disclosed the enormous service to the public which this Bureau has rendered per dollar of taxpayers' money which has gone into the service as a result of efficient organization and particularly because of the friendly contribution of services by an enormous number of voluntary meteorological observers organized by and cooperating with the Weather Bureau. It was evident, however, that a new technique of weather forecasting, based on "air mass analysis" and which originated in the Scandinavian countries, has proven to be superior to the older method now in use by the Bureau which was based essentially on a systematic study of precedence in weather maps. The air mass analysis method is a three-dimensional rather than a two-dimensional study of the atmosphere and therefore involves the use of meteorological data taken at high altitudes as well as those taken on the surface of the ground. The atmosphere is like a huge ocean with cold currents coming down from the north, warm, humid currents flowing up from the region of the Caribbean, and a third current flowing in from the Pacific. These currents are like great rivers, or like the Gulf Stream, in the atmosphere and follow more or less well-defined but continuing varying paths over the country. Storms and quick changes of temperature occur where they meet. Tests on the Atlantic coast by the Massachusetts Institute of Technology, and on the Pacific coast by the California Institute of Technology, and some years of use by the military services, have demonstrated the improved accuracy of this new method. While greater accuracy is valuable for all human activities which depend on the weather, and economically important, particularly in the handling and transportation of foodstuffs and livestock, it is the requirements of modern commercial aviation which have rendered acute the problem of greater accuracy in weather forecasting.

We found that all of the governmental agencies involved were anxious to cooperate in any movement which might improve the work of the Weather Bureau. The Army and the Navy offered to assign some of their airplanes, used in practice flying, for the purpose of taking up to high altitudes the self-recording meteorological instruments needed to secure the data on temperature, pressure and humidity, and to do this at strategically located stations over the country. The Bureau of Aeronautics in the Department of Commerce agreed to cooperate more closely with the Weather Bureau in unifying the communication system for transmitting meteorological data. The Board therefore recommended the adoption of the air mass analysis method of forecasting, together with other important improvements, such as increasing from two to three, and if possible four, the number of daily weather maps, the attaining of an increased amount of meteorological information from the region of the Caribbean Sea in which destructive hurricanes have their origin, and the closer inspection of meteorological stations.

These recommendations have been adopted and are being put into effect as rapidly as circumstances permit. The major difficulties to be overcome are first, the re-training of personnel to use the new method, which will take a minimum of five years and which involves some knotty problems of internal administration, and second, some increase in the annual appropriations to the Weather Bureau, which can be unquestionably defended on the ground of large economic return to the country but which are difficult to obtain in these times of anxiety over federal expenditures.

Another great and essential scientific service of the Federal Government is the United States Bureau of Standards through which are maintained those scientific and technical standards which form the very basis of modern manufacturing methods, as well as of scientific and technical work generally. A peculiarly acute problem faces the Bureau of Standards because of the following situation, which is over and above the problem of decreased budgets which has faced the scientific services generally.

Because of the nature of the Bureau of Standards, it has been found to serve a useful purpose in setting the specifications for the purchase of all kinds of materials by federal agencies, such as army blankets, trucks for the Post Office Department, thermometers for the Veterans' Hospital, and thousands of similar items. Having set these specifications, it is then necessary for the government to test its purchased materials to find out whether they meet the specifications, and here again the Bureau of Standards has been found the most convenient, and in fact, the only government agency set up to make such tests. Consequently a very large portion of the work of the Bureau has come to be the testing of purchased materials for other branches of the government, although this work was not contemplated or provided for in the Organic Act which created the Bureau. As a matter of fact, nearly half of the budget of the Bureau of Standards is required to carry on such work.

When the severe reductions in appropriations to government bureaus were made for the purpose of balancing the federal budget, the total appropriations to the Bureau were cut nearly 50 percent. It was impossible, however, for the Bureau to reduce its expenditures for these government testing services because the government was continuing to purchase materials even on an increased scale. The fact that the Bureau has had to continue this work undiminished has resulted in its crowding out a large portion of the proper work of the Bureau for which it was originally established, and this work, as a matter of fact, has had to be reduced at least 70 percent. The problem of the Bureau of Standards has therefore been one of the most severe of any of the federal bureaus.

Three agencies have combined to make a joint study of this situation, the Science Advisory Board, the Visiting Committee of the Bureau of Standards which was set up by Act of Congress, and the Committee of the Bureau of Standards of the Business Advisory and Planning Council of the Department of Commerce. This joint committee has made a detailed study of the activities and problems of the Bureau and has recommended that certain activities be dropped, that others be transferred to non-governmental agencies where possible, that others be reduced for the time being, and that still others be pushed

forward and extended. Many of these recommendations have not been made because reduction or curtailment was desirable, but simply because such curtailments had to be made somewhere because of the budget reduction.

The Secretary of the Interior asked the advice of the Science Advisory Board as to whether the Geological Survey and the Bureau of Mines should be combined or retained as separate bureaus. A study of the situation led to the recommendation that the bureaus should be maintained separate, though with minor readjustments of functions. There were two primary reasons for this recommendation, one that the objectives and methods of the two bureaus were quite different, and the other that it would be difficult if not impossible to find one director for the combined services who would be sufficiently acquainted and sympathetic with both of them to prevent one or the other suffering from lack of leadership. At the same time the study disclosed a woeful inadequacy of statistical information in regard to minerals generally, and this at a time when such information is most urgently needed for the administration of the codes of regulation of production and of tariffs and reciprocal trade agreements. It was therefore recommended that the agencies charged with collecting mineral statistics, which are now spread over four bureaus in different departments, should be consolidated into one bureau of mineral economics and statistics. I am glad to say that these recommendations also have been adopted.

The Federal Coordinator of Transportation requested the Science Advisory Board to appoint a committee to cooperate with a committee of railroad presidents, for the purpose of finding out whether the railroads are making as effective use as possible of modern scientific and technical developments, and to formulate a plan whereby the railroads may make as effective use as possible of such developments. This joint committee of leading railroad presidents and distinguished directors of industrial research has rendered its report in which broad policies for guiding and coordinating research work for the railroads were laid down. The results of this report are being crystallized in the newly formed Division of Planning and Research of the Association of American Railroads. There is no doubt but that the opportunities here are great and that the railroads are disposed to make every effort to utilize modern technology as effectively as possible, and it is perhaps fair to say that it is the human element in the situation, namely, the difficulty in finding properly qualified men to take charge of this work, which will be the limiting factor in the rate at which this program will be made effective.

One of the possible cures for the depression which has frequently been suggested is the creation of new industries, and the Secretary of Commerce has requested his Business Advisory and Planning Council and the Science Advisory Board to cooperate in recommending to him a program to this end. The assignment is a difficult one, for new industries are like babies—they need shelter and nourishment, which they take in the form of patent protection, financing, and chance of reasonable profits. But, before all, they need to be born, and their parents are science and invention. Neither laws, nor committees, nor juggling acts can perform the necessary first step of conception. Also, like babies, new industries require time for growth. It is therefore evident that consideration of this problem involves stimulation of scientific

research and engineering development, requires opportunities for financing and for the making of progress, which are rendered somewhat difficult under some of the more recent legislation, and requires a degree of patent protection which is difficult under our present system which is staggering along and almost swamped by the complexity of modern developments in the patent fields of types which were not contemplated when the patent law was originally drawn.

To cope with this situation the Science Advisory Board is making certain recommendations of government assistance in the stimulation of scientific work generally, and is submitting recommendations for certain modifications in patent procedure which should greatly improve the present situation without changing the general structure of patents. Some of the situations which these recommendations are designed to meet are the following.

The load on the Patent Office, from the enormous number of applications to patent all things from the trivial to the important, is such that adequate examination of priority is impossible. For this reason the assurance of a patent does not now carry with it the proper validity and, in fact, about 8 per-cent of all patents which come up for litigation are declared invalid by the courts. The situation is so bad that it has come to be said that a patent is simply an invitation to sue.

A second difficulty lies in the time and expense and doubtful outcome of patent litigation. The expense has become so great that some large organizations are seriously questioning whether or not their research organizations are an economic gain or loss, and others are avoiding patents and seeking security and secrecy.

A third difficulty lies in the complexity of modern invention, whereby a single product may involve a large number of different patents often held by different individuals. If any one of these individuals refuses to grant license under his patent, he may entirely block production of the product. It is this situation which has forced organizations to seek to acquire patent monopolies which in turn have not been looked upon with favor by the courts. The situation is well nigh an impossible one in its present form.

Through wide consultation and correspondence, a general consensus of opinion has been found in support of certain remedies for these situations, and these will soon be submitted to the Secretary as a partial answer to his request for a plan for the stimulation of new industries.

One of the most far-reaching services of the government is its work in surveying and mapping. An accurate map of the United States is a pre-requisite of all types of construction and planning. The standard map of the United States is less than half completed and until the work is finished millions of dollars will be wasted in temporary and uncoordinated surveys which are found necessary by municipalities, or states, or construction agencies, to handle their particular jobs. We are the only important nation in the world whose country has not been adequately surveyed and mapped.

There are more than twenty bureaus in the government which have mapping activities. The question has frequently been raised, "Should not these be consolidated?" This question has been investigated by the Science Advisory Board at the request of the Director of the Budget and a report with recom-

mendations has been submitted to him. Among the interesting considerations are the following.

In some bureaus the production of maps is not a major objective but maps are produced and used only as tools in the attainment of some other objective. In the case of other bureaus, however, the sole purpose of the bureau is to produce maps. As a basic principle it may be suggested that the tools should not be taken away from the people who need to use them. In other words, the subsidiary mapping services should not be consolidated into a federal bureau. On the other hand, a strong argument for efficiency can be made for the consolidation of those services whose sole objective is the production of maps. This argument is based upon efficient use of personnel the year round, elimination of duplication and uniform adoption of the most modern and efficient methods. On the other hand, there may be good reasons for the maintenance of separate units in several cases. For example, in the military services, where military necessity, or secrecy, or the maintenance of a staff under immediate military control, may be important factors.

This question has been frequently discussed by previous commissions and before Congress, and there are amusing illustrations of arguments pro and con which have been invented to impress Congress without adequate basis of fact. From the standpoint of national efficiency it is highly important that some action should be taken, but any action which involves the transfer of established bureaus meets with a type of opposition which is politically difficult to overcome. We very much hope that the present effort may meet with a degree of success which has been denied the more than a dozen previous efforts which have been made to effect an improvement in this field.

It has been very difficult to secure an unbiased opinion regarding the economic possibilities of mineral development in the region of Boulder Dam with the utilization of the electric power there developed. Perhaps because of the great industrial and political interests involved, the Science Advisory Board was called upon as a disinterested body to make a survey and report on this matter. This work was carried out in three steps: First, a factual survey of the extent, grade and accessibility of the mineral deposits within reach of electric power in the Boulder Dam; second, a determination of the cost of production of the various products obtainable from these mineral deposits; and third, a consideration of such economic features as transportation costs to the point of demand and the effect of such production on similar industries in other localities. The result of this study has been the publication by the Department of the Interior of a factual analysis from which can be selected those products which can profitably be developed and those other products whose development at the present time would be economically impossible in competition with other sources of supply.

The Department of Agriculture carries on more scientific work than any of the other departments. This work is found in about ten out of the eighteen bureaus of the department. Many of these bureaus are almost independent organizations and there is a considerable amount of duplication of effort and of facilities. Some of this duplication is necessary to the efficient performance of work, while in other cases a more effective coordination would undoubtedly

be advantageous. The Secretary of Agriculture requested the Science Advisory Board to give particular attention to the Bureau of Chemistry and Soils in its relation to the chemical work of other bureaus. It has sometimes been suggested that all chemical work of the government should be concentrated in one comprehensive bureau of chemistry. On the other hand, it is pointed out that chemistry is frequently a tool which is needed by a worker in some other field where the objective is not primarily chemical in nature. It is obviously a very difficult matter to ascertain the most effective degree of consolidation or the best type of coordination of such work. A distinguished committee has been giving attention to this problem, bringing in the benefit of the best industrial experience as well as expert knowledge of chemistry. This committee has found certain difficulties which are peculiar to the government organization and which probably preclude an ideal solution to the problem. In view, however, of the millions of dollars which are spent on research in this department, it is decidedly to the public interest to see that this work is being done with the maximum effectiveness, and the officials of the department are cooperating with the committee in an effort to find a solution which will be as nearly ideal as possible and at the same time practicable within the limitations of government operation.

These illustrations, taken from the varied activities of the Science Advisory Board, will show something of the interest as well as the complexity of the government's work in the varied fields of science. Beyond these particular services attached to existing bureaus, there lies, however, an immense field of government responsibility in which science plays or may play a prominent part, and I would next comment briefly upon the opportunities and responsibilities which the government may have in this larger field.

There are important national problems like insanity, crime, public works, unemployment, excess agricultural production, land use and power utilization, which are of great concern to government but for which the responsibility extends beyond the jurisdiction of governmental bureaus to states, municipalities and to the people as a whole. They involve considerations of care, relief, control and management which are the subject of governmental action involving enormous expenditures. They are the concern of the social scientists in order that this care, relief, control and management may be wisely conceived and administered. But they should also be the concern of the natural scientists in two main aspects: first to ascertain the facts which are susceptible of scientific observation or measurement, in order to supply social scientists and government with data essential to their activities; second, to alleviate or cure the difficulties where this is possible by applications of science, as illustrated below.

The magnitude of the purely economic aspect of these problems is realized by very few people. In the case of mental illness alone, approximately 20 per cent of state budgets goes to care of the mentally diseased. Past experience and present knowledge both indicate that science will probably succeed in alleviating or partially curing all of these difficulties if given adequate time and opportunity. It is obviously in the public interest, therefore, that this opportunity should be given and that this should be done as rapidly as the scientists themselves are able to handle the opportunity. As an investment for the future

or an insurance against future expenditures, and at the same time as a social obligation, the government has a great responsibility in seeing to it that work along these lines is pushed as vigorously as possible.

The Science Advisory Board is prepared to cooperate with other agencies in pointing out this responsibility and urging that the government accept it.

If time permitted it would be possible to analyze these problems in greater detail and to submit specific programs for work in pure and applied science whose social value is unquestioned and which can be laid out with some degree of assurance on the basis of present knowledge. I would simply mention, by way of illustration, such matters as tropical diseases, long range weather forecasting, development of new and improved uses of electric power, discovery of new uses for agricultural products, elimination of specific hazards in navigation, etc.

It is interesting and somewhat disheartening to note that our country, with all of its boasted progressiveness, has paid less attention to science as a means of combating our present difficulties than any of the other great powers.

Russia, seeing what science has done in raising the standard of living in other countries—especially in our own country—is centering her whole economic program on science. She has used, as the central feature of this program, the Academy of Science, founded by Peter the Great. Under this have been established more than two hundred great research institutes for work in pure science and engineering. Her annual appropriations for these institutes are reported to be larger than any other item in her budget—even the military and defense item.* Many of her scientific laboratories rank among the best equipped laboratories in the world at the present time. Though short of trained workers, they are already turning out some first-class work, and a well-considered program of selecting and training research workers has been instituted.

Great Britain also has taken decisive steps to utilize science for social and economic improvement, despite the fact that she was harder hit than we by the war, her unemployment crisis came sooner, her taxes are higher. She has called her leading scientific men to advise her Privy Council on scientific and technical policies, through three Advisory Councils composed of Britain's most noted scientists. It is on advice of these councils that the programs and budgets of the government's scientific bureaus are determined. The government, furthermore, appropriates about a million pounds annually, to be used for research. On advice of the Advisory Council, appropriations are made to governmental scientific bureaus and grants for research are made to educational institutions and scientific societies; also for research fellowships, and for support of industrial research by trade associations provided these associations match the grants with similar contributions from their own funds. In this latter way, programs of research have been inaugurated in twenty-one of the most important industrial associations.

Italy has mobilized her research facilities in a broad-scale effort to rehabilitate her economic position, and to counteract her deficiency in raw

* Report by Dr. Julius F. Hecker of Moscow University, who was sent to the United States to arrange for a system of exchange research professorships between the United States and the Soviet Republic.

materials through application of her "brain power" to the most effective use of what she has. The government has appropriated large sums for the better equipment of university research laboratories, and all work in these institutions and in governmental laboratories is supervised by a National Research Council. Furthermore, no governmental financial assistance is given to industries unless this Research Council certifies that the industry maintains a progressive policy of research and development.*

Until recently Germany led the world in her sustained efforts to maintain a strong economic position through scientific research, notably in the fields of chemistry and metallurgy. Everyone knows the success of this policy, until it was largely wrecked by other circumstances. Her scientific strength, however, is still probably Germany's strongest economic asset.

Japan, for years, has been bending every effort to introduce western technology into her industrial procedures. Begun as a policy of copying technical processes and products which had been developed elsewhere, it was accompanied by an intensive program of scientific education of her own scholars. She is now in a position to lead as well as to follow in scientific work of high quality, and this is bearing fruit in her industrial position.

Compare this picture with that of our own country. As soon as we got into trouble we cut our governmental expenditures for scientific work *more* severely than those of any other government activity. We gave no consideration either to unemployed scientists or to the public value of their work in our emergency measures for relief of unemployment or for economic rehabilitation. And yet we have prided ourselves as being the most advanced nation on earth.

The truth is that we have been fortunate enough to have great natural resources, which we have exploited riotously; we have had a pioneering spirit which has bred some great inventors; this same pioneering spirit has developed some industrial giants who have plunged into big things and have brought "quantity production" into operation; we have been blessed with a few great philanthropists whose altruistic vision has led them generously to support scientific work and other activities for human welfare in universities and other private institutions. But, as a people and therefore as reflected in our national policies, we have been more lucky than intelligent. Now that we are no longer able to thrive on the unrestricted exploitation of the gifts of Nature, it is imperative that we take steps to utilize our resources more intelligently and effectively—and this means scientific research on an increasing scale.

In conclusion it seems to me that what is needed is a bilateral program for putting science to work for the national welfare. There is needed on the one side the cooperation of the scientists of the country generally, to assist the government in putting the work of its scientific bureaus on a scale of maximum efficiency and value. There is needed on the other hand a new type of government leadership whereby the scientific men of the country may be brought together to make an intelligent and coordinated attack on the great problems

(*Please turn to page 117*)

*** Report by Mr. Maurice Holland, director of the Division of Engineering and Industrial Research of the National Research Council, following his recent study of conditions in Italy.**

GENETIC CONSTITUTION AS A FACTOR IN DISEASE*

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From the modern viewpoint, disease may be regarded as the resultant of three factors: (1) the constitution of the host, (2) the disease-producing entity, the pathogen, (3) the environment, which, in a broad sense, may favor either pathogen or host or both in so far as susceptibility, severity and mortality are concerned. The time for emphasizing the inter-relation of these three variables has, perhaps, arrived. Yet this has not always been true. Rather, in the unfolding of medical thought, have they been as parallel threads, the strength now in one, now in another, according to the age. The time and place of their origin are, however, unknown to us. They may have risen among other ideas which we now discard as, for example, the power of Apollo's darts in inflicting epidemic disease on the army before Troy. Even in our earliest known writings on disease are references to the supernatural. The Erwin Smith Surgical Papyrus[1] (written not later than the Seventeenth Century B.C., and from internal evidence probably copied from material dating back to 2500-3000 B.C.) discusses from a thoroughly modern outlook forty-eight cases dealing with wounds of mechanical origin and follows this with eight mythical incantations against an annually recurring disease designated "the pest of the year." Here are suggestions that the pest may enter through the mouth and throat, that flies may carry the pest, that it may be borne by the wind or be lurking in food, bedding or other household articles. But these ideas are so mingled with a mysticism quite different from the straightforward scientific treatment given the surgical cases that the real state of knowledge can only be surmised. Yet only slightly later evidence seems to justify our assumption that contagion was recognized as a factor in disease during this age for in Leviticus, among certain laws and precepts now seemingly fantastic, we have a description of the procedure to be followed in renovating a house which has been occupied by a leper. Another doubt, however, assails us here. Were these pronouncements the words of the priests presenting religious ideas, or do they reflect the strictly scientific knowledge of the day? It is impossible to say. All that is known is that although the idea of contagion recurred from time to time in the writings of lay historians and poets, it did not gain a foothold in biological thought. It was rather an idea complete in itself but too premature to have further effect on the contemporary scientific ideas. Only later rediscovery, in a more complete setting, allowed it to take its proper place in biological thought.

The idea of constitution as a factor in disease suffered no such fate. We find, in books attributed to Hippocrates,[2] opinions revealing a clear appreciation of the significance of genetic constitution in disease. It is no passing reference, it is woven into these books as a connecting thread. Ancient Medicine, Epi-

* This paper is a part of an address to the Princeton Chapter of Sigma Xi.

demics, Airs, Waters and Places, etc., all describe it. Possibly the best portrayal is found in the book devoted to Sacred Diseases. The sacred disease V.: "But this disease is in my opinion no more divine than any other; it has the same nature as other diseases, and the cause that gives rise to individual diseases. It is also curable, no less than other illnesses, unless by long lapse of time it be so ingrained as to be more powerful than the remedies that are applied. Its origin, like that of other diseases, lies in heredity. For if a phlegmatic parent has a phlegmatic child, a bilious parent a bilious child, and a splenetic parent a splenetic child, there is nothing to prevent some of the children suffering from this disease when one or the other of the parents suffers from it; for the seed come from every part of the body, healthy seed from the healthy parts, diseased seed from the diseased parts. Another strong proof that this disease is no more divine than any other is that it affects the naturally phlegmatic, but does not attack the bilious. Yet, if it were more divine than others, this disease ought to have attacked all equally, without making any difference between bilious and phlegmatic."

In the 500 years between Hippocrates and Galen schools for the study of disease appeared in widely scattered localities. The philosophical background for each school became more or less distinct, anatomical and physical considerations possibly receiving most emphasis. To Galen, in the Second Century, we owe the compilation and critique of these scattered fragments of the earlier thought as viewed through the eyes of a protagonist. He held that the generation of herd sickness depended upon the inter-play of three factors: an atmospheric factor, an internal factor, and an external factor. In a modern sense the first of these factors seems to have little meaning. The second factor, the internal, would seem to include the genetic constitution of the host and the experiences or environment to which this host was subjected nearly up to the time that the disease appeared. By the third or external predisposing factor is meant the effect of the more immediate environment, such as habits of life, eating, drinking, etc., on the transmission, spread, and severity of the disease.

The precise Euclidean logic with which Galen organized and supported these concepts furnished the necessary impetus for their perpetuation. For nearly 2,000 years the significance of constitution in disease found repetition in medical literature as the Hippocratic corpus became dominant in the study and treatment of disease. It is difficult to evaluate the progress which was made. Certainly the concept was far too general. It needed a searching scrutiny to break it into parts and give it meaning. But inquisitive thought apparently had stagnated. Our second thread representing genetic constitution had to be broken and temporarily lost to medical science. In the interim before its rediscovery the ancient concept of contagion was revived and the idea of a contagious principle, self-reproducing and perpetuating, became dominant. Meaning, however, was to be put into the second factor, the host's genetic constitution, as the result of a paper buried in the literature, although published in 1865. The work of Mendel[3] had that simplicity of expression which so appeals to the mathematician. He chose alternative characters in the garden-pea for his study and showed, for instance, that the difference between a seed with yellow and one with green coat-color could be attributed to two

distinct entities which we now call genes. The viewpoint toward inheritance like that toward matter had become particulate. It was evident that the structural entities which brought about the particular character were distinct from each other. The genetic constitution was shown to be due, not to a general over-all character as Galen's internal factor or crisis might be interpreted, but to the interaction of many separate entities. Good working concepts thus had been formed. Mendel's work gave the same stimulus to the study of heredity that the atomic theory did to the ultimate constitution of matter, the same impetus as the particulate theory of infectious diseases gave to pathology. But its significance was passed by unnoticed for thirty-five years.

It seems unlikely, as we see it now, that the discovery of Mendel's papers of 1865 and the presentation of DeVries' mutation theory[4] would create any stir in the pathology of 1900. The yellow color of peas could scarcely be considered a pathological form of the green variety since both seemed to be of similar viability. It was true, however, that certain of the evening primroses that DeVries worked with showed 50 percent or more pollen death. Whatever Mendel's discovery may have done to pathology, the relation of morphology to disease, it did lead immediately to a great scientific truth relating morphology to normal structure. It led directly to the observation by Sutton[5] that the behavior of chromosomes in preparation for the union of egg and sperm was such that the chromosomes should be bearers of the inheritance, the genes. This conclusion, that the chromosomes are the bearers of the specific elements of the inheritance, the genes, came as a great awakening, for in it lay the secret of much of the development which later followed. It led to theories of sex-linkage, of crossing over, or chromosome interchange, and of non-disjunction, to mention but a few of the earlier advances. Some idea of the manner in which these observations have been related to pathology are reviewed in the succeeding paragraphs.

HOST RESPONSES TO INFERIOR GENETIC CONSTITUTIONS

A significant example of the part that genetic constitution may play in pathological conditions is found in the observations of Cuénot[6] on mice of yellow coat-color. The yellow mice differed from most of the others in the fact that when they were bred together some of the progeny always showed a non-yellow color. The ratio of yellow to non-yellow in the progeny of two yellow mice was 2:1 instead of the 3:1 which would be expected if yellow were a dominant factor and the yellow mice were Yy. Again if yellow mice were bred to non-yellow, progeny having either yellow or non-yellow coat-color were obtained in nearly equal proportions. This is the proper expectation if the yellow mice were of Yy and not of YY composition. But what became of the YY progeny which would result from a cross of two Yy animals? Histological investigation of the uteri of yellow mice bred to yellow males showed that the death of the YY embryos occurred early in development, at about the time of implantation. The internal organization of one embryo, even to one of its single entities, was capable of ending the life it had a part in beginning.

The principle that genes cause differences as extreme as those noted in the yellow mice is now well established. This is due partly to the fact that all lethal or semi-lethal genes do not kill the host at the same stage in development. Lethal anemia in mice, due to the dominant white spotting gene, is one example. The existence of this gene was first noticed by Little[7] in 1915 when dominant white spotting was observed to give recessive lethal effects. Further study by Detlefsen,[8] De Aberle[9] and myself[10] has shown that death occurs just after birth. The mice which are to die, since they are homozygous for the lethal gene white spotting, show a severe anemia, the hemoglobin being but one-third that of their healthy litter mates. That death is due to the deficiency of hemoglobin is proven by the fact that the injection of blood from normal mice will prolong their lives and enable them to survive for fairly long periods of time.

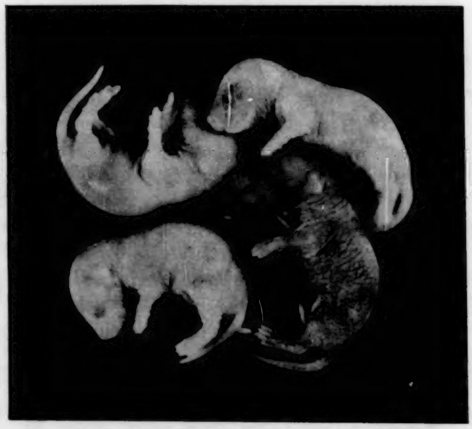

FIG. 1. A litter of mice at birth, containing three anemics and one normal. The parents were heterozygous for the gene causing the anemia.

Cases like those cited above, in which the internal or crasis factor of Galen is alone responsible for a certain pathological condition are becoming increasingly common as the study of genetics penetrates the physiological basis of pathology. Our observations show that deaths and abnormalities are often centered about critical stages in developmental processes when the organism changes from one type of life to another, as for instance the time of hatching in oviparous animals or of birth in viviparous species. The fact that deaths are noted at such periods does not necessarily mean, however, that the lethal effect of the gene was coincident in time with the death of the animal. Nishikawa[11] in a study of the silkworm described the effect of seven lethal genes which ostensibly killed in the egg stage. The first of these genes killed in the early stage of segmentation. Five other lethals retarded embryonic growth so that the eggs did not hatch. The seventh gene allowed the larva to

grow normally for three or four days, when retardation appeared. Death occurred between the tenth and fifteenth days after hatching.

This variability in time and place effects is well illustrated by lethal genes in cattle. The gene which in heterozygous condition determines the characteristic short legs and body form of the Irish Dexter cattle, when homozygous produces monsters strikingly defective in many particulars, *e.g.*, the pituitaries.[12] Death occurs early in embryonic development. A gene, occurring in a Norwegian breed, produces similar effects,[13] achondroplasia, bull-dog head, split palate. Such animals may come to term. With still another lethal[14] the calves are born but the skin of the extremities and mucous membrane of the mouth are defective. Death is accompanied by a septicemia thought to be due to bacterial invasion through these open areas. Other lethals produce hairlessness, amputation of the extremities, foreshortening of the skeleton with fusion of the rudiments and prenatal cataract of the stellate type.[15]

Such are the known cases for one species. Other species have similar numbers, although the number is apparently limited only by the amount of study which has been devoted to the particular group. Genes may alter many kinds of structures and thereby affect physiological functions as well, *e.g.*, basal metabolism,[16] utilization of vitamin D,[17] etc. Thus the genes are capable of creating profuse and diverse pathological conditions in their own right without the intervention of other agencies.

GENETIC CONSTITUTION AND INFECTIOUS DISEASE

As genetics has progressed observations have been accumulating which, though different in detail, all point to the genetic constitution of the host as a causal variable in infectious diseases, as well as in those dependent on obvious structural alterations. For example, rust of wheat was thought to be due to a specific agent, a fungus, as early as 1797. Varietal differences in susceptibility to this disease were established by 1841 and Biffen[18] in 1905 published a paper in support of his theory that resistance to the striped rust fungus of certain varieties depended upon a single gene. This paper was followed by others in which single pairs of genes were shown to be responsible either for the death or for an almost complete immunity of a host species as in Walker's[19] study of fusarium wilt of the cabbage. In other diseases the resistance depended upon a more complex genetic constitution.

The work with animals, presumably because of its inherent difficulties, does not supply us with such a wealth of cases as does that with plants for the demonstration of similar genetic principles. A few well-studied instances suggesting future trend, however, are available. The epidemic disease of mice due to *B. piliformis* almost invariably attacks one species, the Japanese waltzer, the common type being resistant. Crosses between two species are, in general, resistant. The second generation backcrosses and F_2's segregate in a manner suggesting a single Mendelian factor difference as the cause of the inheritance of susceptibility and resistance.[20] A second instance is found in the work on guinea pigs. The blood of these animals typically is rich in compliment, a substance which plays a part in certain biochemical reactions related to immu-

nity. This compliment was found by Rich[21] to be nearly absent from certain Vermont guinea pigs. Genetic analysis of the two types showed that the compliment-deficient animals differed from the normal by one pair of genes—the compliment-deficient pigs were homozygous recessives, the full-compliment pigs were heterozygotes or homozygous dominants. In a spontaneous epidemic in which *B. suscepticus* appeared in these stocks, the compliment-full pigs often developed lesions of the liver, spleen and peritoneum but seldom died. A large part of the low-compliment pigs, on the other hand, died so suddenly that they did not develop the lesions which characterized the disease in the more resistant normal animals. The focus of the epidemic was the deficient-compliment pigs. An experiment to test this matter further was performed. One hundred pigs of each group were inoculated with living *B. cholerae suis* under similar conditions. Of the 100 compliment-deficient pigs only 23 survived at the end of forty-eight hours; of the normal, full-compliment pigs 80 were alive.

The necessity for cooperation between the genetic constitution of the host and the pathogen in the production of disease has been shown for many pathogens and hosts. Diseases due to certain bacteria, fungi, protozoa, helminths, viruses and chemical poisons have shown differences in severity attributable to the genetic constitution of the host. Such effects are in no way different from those in which the abnormality is caused by the action of the genetic constitution without a pathogenic agent. This genetic constitution conceivably could be either a single character of the nature of Galen's crasis factor which enables the organism to resist a multiplicity of environmental agents or a composite of many independent characters each of which is capable of causing the individual to resist one environmental agent. The fortuitous combination of these characters thus could make animals resistant to many or to few agents.

Data taken from the work of my former colleague, Doctor Schott and myself on these inbred lines of mice and their crosses are pertinent to this problem. It is well known that repeated mating of brother to sister carried over a number of generations tends to make the progeny of such matings more and more alike. Although the animals within any particular line of mating are becoming more and more alike, the different lines which are established are becoming more diverse. By analogy, a line which may be regarded as a mixture of genes can be compared to a mixture of different chemicals, each with its own characteristic properties. By suitable procedures these chemicals may be separated, *e.g.*, the molecules of bromine from those of chlorine, etc. Subsequently the different kinds of molecules may be compared with reference to their reactions to any other. The constitutional differences of the mouse population may likewise be split into relatively pure groups and these groups compared with regard to their reaction to different diseases.

These genetically different lines of mice were available for this comparison. These different strains were tested for their reactions to three diseases: mouse typhoid by Schott, a virus disease-pseudorabies, and an antigenic poison, ricin, by Schott and myself. Graphs on the arithlog grid, showing the survival rates of these different strains are presented in Figure 2. The pseudorabies plot shows that the S line is quite susceptible while the Sil and W. F. lines

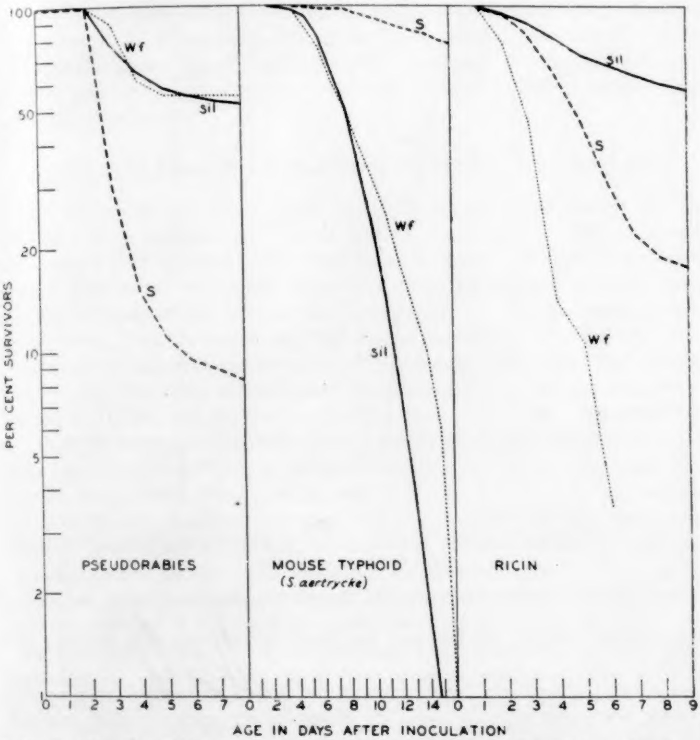

FIG. 2. Survivorship curves of the S, Sil and W. F. strains of mice for the virus disease, pseudorabies, the bacterial disease mouse typhoid, and the antigenic poison ricin (males).

are both quite resistant. For mouse typhoid the reactions are reversed. The S stock is resistant, whereas the Sil and W. F. strains are quite susceptible. In the case of ricin, the Sil line is most resistant, the S is susceptible, and the W. F. is nearly wholly susceptible. The genetic constitution for resistance is evidently specific for the material and strain. From this it would seem that constitution in general is, like other characters, dependent upon the interaction of specific genes rather than upon an over-all type of reaction.

The survival curves of crosses between two of these lines, Figure 3, furnish further evidence in support of the foregoing view. In the case of pseudorabies, the F_1's are intermediate between the parental lines but somewhat closer to the susceptible S parent. What dominance there may be is toward the susceptible side. In typhoid, however, the F_1 is essentially like the resistant parent. There is, in the case of ricin, a marked difference in the reaction of the two sexes. This ultimately would be attributed to the difference in chromosome balance in the two sexes. The F_1's whether male or female show a marked resemblance

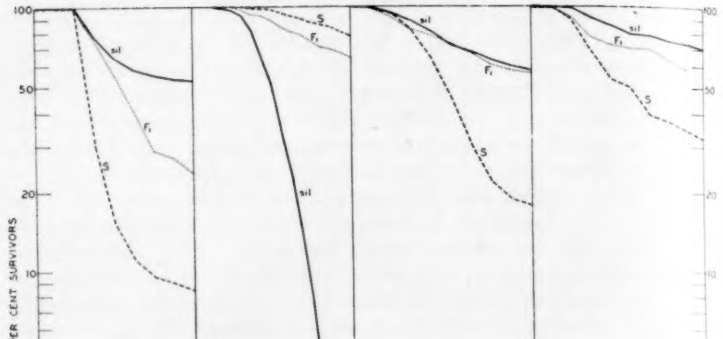

FIG. 3. Survivorship curves of the S and Sil strains of mice and their F_1.

to the resistant parent, not however the same parent that was resistant to the typhoid.

The effect of the genetic constitution on the clinical and pathological symptoms of disease are essentially the same for plants as for animals. For example, a single gene may confer immunity or resistance to several pathologic forms of rust or it may limit itself to one form. Resistance to several diseases, in general, results from the chance collection of genes, each of which has a specific effect on one disease, the combined action of these genes being necessary for resistance to all of the diseases. This specificity may be so exact as to differentiate not only diseases but strains of the same disease. Resistance to anthracnose in the bean plant has been shown by McRostie[22] to be equally dependent upon the genetic composition of the bean host and the anthracnose organism, *Colletotrichum lindenuthianum*. The alpha strain of the anthracnose infects only plants homozygous for the recessive alpha gene. The beta strain of anthracnose infects only plants homozygous for another recessive, the β gene. To this group Burkholder[23] added still another strain of anthracnose and the gene for resistance to it, the gamma. It takes the combination of all three of these genes to make a plant resistant to anthracnose in general, the combination and permutations of the three genes and the three strains of the disease making the plants resistant to none, one, two, or all three strains.

The foregoing facts demonstrate the specific nature of genetic resistance of the host. The particular clinical and pathological symptoms are often an expression of the host's inheritance rather than the variability of the pathogen.

The observations from which these deductions are drawn are far more numerous than here indicated. From them we may derive our second principle, the segregation of specific genes for susceptibility and resistance to disease initiated by pathogens may be responsible for immunity, morbidity, or mortality within the exposed population.

GENIC BALANCE IN RELATION TO DURATION OF LIFE

Up to this point the genetic constitution in its effect on disease has been considered only in terms of its ultimate entities, single genes. The pathological changes which they produce when they react in groups or when their normal balance is distributed are equally important. Sex furnishes a striking illustration of the influence of this balance of the genes. In the fruitfly, males have one X-chromosome, Y-chromosome and two sets of autosomes, whereas the females have two X-chromosomes and two sets of autosomes. Since the Y-chromosome is largely inert, the ratio of sex-linked to autosomal genes in the male may be expressed as X/2A, but in the female this ratio is 2X/2A. Aberrant forms with other chromosomal balances have been found[24] and life studies on two of these have been made[25]. One, having three X-chromosomes and three sets of autosomes, is a typical female except that the cells of the body are somewhat larger than usual. Another form has two X-chromosomes and three sets of autosomes. Such flies are neither sex but have vestigial organs of both sexes. By suitable genetic technics it is possible to obtain these types in large numbers. The effect of this alteration in the genic balance on the ability to survive under what were intended to be the best conditions is shown in Figure 4.

The types in which the X-chromosomes and autosomes are balanced, the normal females and triploids, show the greatest survival. The unbalanced type, the males, are shorter lived. Intersexes with the two sex chromosomes to three sets of autosomes, and the consequent extreme internal modification of their organs show a still shorter length of life.

Similar lethal or semilethal effects as a result of altering the genic balance have been noted in super-females in which the constitution is three sex chromosomes and two sets of autosomes. Varied types of chromosomal reorganization brought about by radiant energy and the accompanying disturbance in genic balance show similar abnormalities resulting in shortened life. The third principle by which the genetic constitution affects the organism may be summarized as follows: The balance in the proportion of the genes composing the body cells may become the etiological agent of a definite pathological syndrome.

THE ORGANISM AS A WHOLE AND THE GENETIC CONSTITUTION OF ITS CELLS

The philosophy of Hippocrates stresses the doctrine that the reaction of the organism as a whole represents more than the summation of the functions of its parts. The implications of such a concept suggest certain questions in regard to the reaction of the host to pathological conditions. How do the genes in particular cells manifest their activity with respect to the organism as a whole? How does the organism as a whole function when part of it is

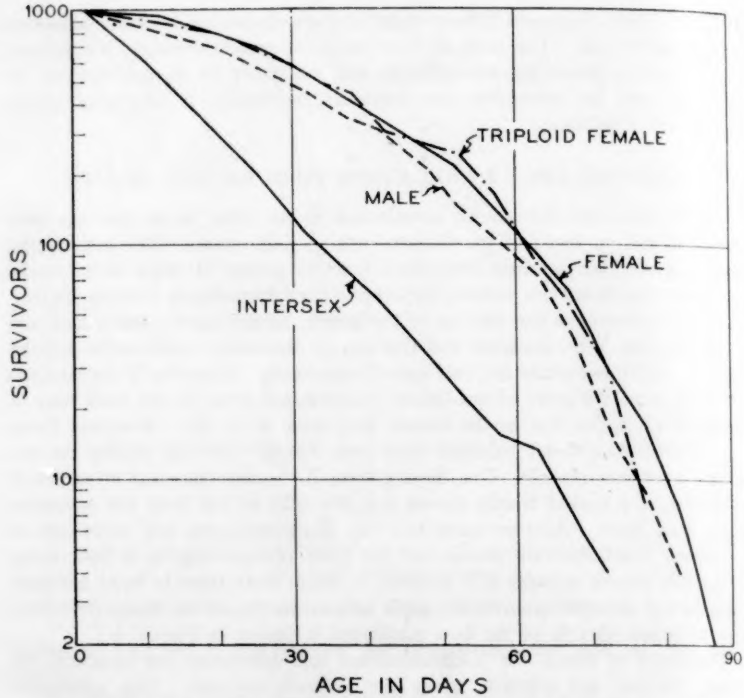

FIG. 4. Survivorship of Drosophila for groups having an altered genic balance within their cells.

of one genetic constitution and another part of a different one? Plant material offers particular advantages in clarifying this problem since by grafting or budding it is possible to join two or more genetically different parts into one functioning whole in such a way that the parts are mutually interdependent. For example, fire blight of the pear, due to *B. amylovorus* is particularly destructive to those varieties which have commercially desirable fruit. Certain Chinese varieties, on the other hand, though immune, bear worthless fruit. Reimer[26] by grafting has made composite trees with roots, stems and scaffold limbs of the immune Chinese variety and tops of the commercially desirable variety. Tests show that although the tops get their sap and mineral food supply from the resistant parts, they remain susceptible and that in spite of the fact that the stem and scaffold limbs get their carbohydrate from the susceptible tops, they retain their immunity. Each part maintains its susceptibility or resistance in accordance with its own genetic constitution, irrespective of the genetic constitution of the other parts. The genes for resistance in the Chinese stock or for susceptibility in the commercial pear are circumscribed in their effect, their action being limited to the cell of which they form a part. These results are

entirely harmonious with those of Patterson[27] and of Gowen[28] who have shown in their work on eye color in Drosophila that the effect of a somatic mutation produced by x-ray is limited tothe altered cells.

In animals it is difficult to obtain two different genetic constitutions fused into a single harmoniously functioning whole. The evidence from studies in embryology favors the conclusion that the somatic cells are identical in genetic constitution. Yet it has been possible to show that when certain types of chromosmal reorganization are produced by x-rays, the somatogenesis may occur in such a way as to produce two or more genetically different types of cell[29] as shown in Figure 5. The mosaic pattern is shown by the two shades

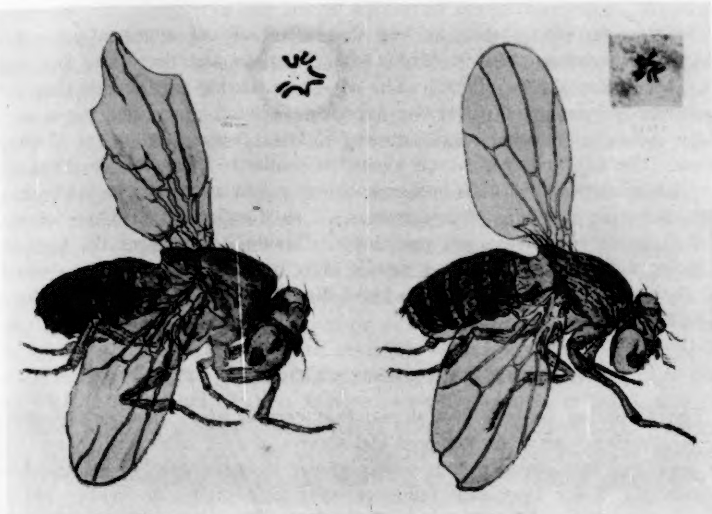

FIG. 5. Male and female Drosophila showing the mosaic of genetically different cells which form the body.

of color in the eyes, notching of the wings, irregular wing veins and bristles in the male. This mosiac condition pervades the whole body. In the males where the testes and Malpighian tubules may be made to show color, the mottling brought about by this dissimilarity of the cells may be seen in clear relief. In every case, the mottling is limited by the cell boundaries, the character of each cell being determined by its own genetic constitution irrespective of that found in the adjoining cells.

The degree, however to which the organism will be a mosaic of one or the other types of cell can be controlled experimentally since the ratio of normal to abnormal cells can be decreased by rearing the flies at a lowered temperature during the first few days of larval life or by adding an extra Y-chromosome. What, then, happens when the portion of abnormal cells increases within the

vital organ? Cases in which all of the cells in the animal are of such an anomalous organization are known to be lethal. Is this constitution likely to cause death if it makes up only a part of the cells, and if normal ones are also present to carry part of the burden of life functions?

When the proportion of abnormal to normal cells becomes large in flies subjected to low temperature, the males die and the number of females is reduced nearly to half the normal controls. Furthermore the surving females are debilitated, sterile in many cases, and live but a short time. If now we reverse the picture by keeping the flies at the higher temperature throughout their life, the mottling is greatly reduced; the males live and breed and the females are essentially normal. Entirely similar results were obtained when the extent of the mosaic was controlled by the presence or absence of an extra Y-chromosome. It is thus evident that a mosaic of abnormal vs. normal cells in an organism tends to hinder vital functions and that when this condition is extreme death follows. The vital functioning of the organism as a whole can be interrupted in varying degrees by a mosaic of genetic constitutions. If the mosaic is extreme, death ensues; if less severe, pathological conditions follow. The effects here observed somewhat similar to those noted by Demerec[30] in which he showed that cells homozygous for a deficiency must be so physiologically defective as to die. Such instances I shall call the fourth type of effect of the genetic constitution on pathology. During development the body, due to its inheritance, may become a mosaic of cells, some normal, some abnormal, and the morbidity and mortality increase directly with the proportion of defective cells in the mosaic.

STRUCTURE OF THE GENETIC CONSTITUTION

The foregoing analysis has shown that certain genes produce a profound effect on embryological development and survival during adult life. These genes are organized into chromosomes which appear to carry most, if not all, of the inheritance. Their significant influence on disease invites an inquiry into the number of genes which are thus gathered together and in their reaction give form to the genetic constitution.

Genes may be classified from several points of view. They may be vital, necessary to life, or lethal; their effects may be external and visible or internal and invisible. Physiologically both members of a pair may have to be present in order to produce an effect, *i.e.*, the gene may be recessive or one member may act by itself—it may be dominant. Under natural conditions genes may change at a slow rate, but such natural mutations are generally lethal. This is true also for mutations produced by x-rays from copper and chromium. Of 302 sex-linked genes mutated from wild stock and having a sufficient number of progeny to determine their lethal effects, 225 or about 75 percent were completely lethal. Less than 3 percent gave to their offspring a viability approaching that of the wild type genes from which they mutated. Out of the total of all sex-linked mutated genes, 364, forty-four produced visible effects and had a viability of 20 percent or more, a ratio of 1:7.3. Muller has published data leading to a similar estimate. Of 128 mutations which were produced by

x-rays from tungsten, he obtained twenty which were at least 10 percent viable and conspicuous, a ratio of 1:5.4. This ratio is somewhat higher than that in the writer's experiment but it also includes a greater number of mutations in the group which survived. The mutations in these experiments were all confined to the sex-chromosome.

The visible mutations of 20 percent viability offer a means by which an estimate can be made of the total number of genes within the sex-chromosome. These minimum numbers would be 132 for the writer's and 120 for Muller's data. The numbers of sex-linked genes of the recessive lethal type would consequently be 7.3 x 132 or 962 for the writer's and 120 x 5.4 or 648 for Muller's data. Besides these methods of estimating the numbers of gene loci in the sex-chromosome, Demerec[30] has introduced another of merit. This method attempts to determine the frequency of mutation for individual genes when they are exposed to a given x-ray dosage. This rate was found to be 2.46 per 10,000. The rate for all genes for the same dose was 1,250 per 10,000 or the number of genes mutating at the 2.46 rate necessary to give the observed total rate is 500. The estimates of the minimum gene loci of the sex-chromosome range from 500 to 962.

The foregoing analysis suggests the manner in which the total number of gene loci within an organism may be estimated. It suffices to say here that depending on certain assumptions the numbers necessary to this small fruit fly seems to be not lower than 2,000 nor more than 15,000. The magnitude of either of these numbers is entirely sufficient to show the complexity and importance of the genetic constitution to the organism. Possibly all of these loci, with their contained genes, are essential. Certainly the rarely occurring natural mutations or the more rapidly produced mutations due to x-rays show that but 8 to 17 percent of these mutant genes are capable of supporting life. The other 83 to 92 percent produce lethal effects on mutation. The fact that every cell making up the body may have two to fifteen thousand distinctly different entities capable of causing death on mutation is further evidence of the intricate balance which nature has established between the organism and its environment. Equally impressive is the fact that individual genes appear not to exceed 1×10^{-16} cm.^{3} in size and very likely are no larger than 1×10^{-18} cm.^{3}, a size comparable with that of large protein molecules.

SUMMARY

Throughout historical thought three general concepts of disease causation have had their proponents. In one case the constitutional origin of disease was stressed, at another agents of environmental origin, and possibly earliest of all contagions or pathogens. Yet by themselves no one of these principles seems adequate. Disease appears rather to be the resultant of the interactions of all three principles. The evidence presented in this paper suggests the manner in which one of these principles, the genetic constitution, influences the end result.

The results show that: (1) genes normal to a species may, by mutation, cause physiological and developmental processes so abnormal that death or

lasting disability results; (2) the segregation of specific genes for susceptibility or resistance to disease initiated by pathogens may be responsible for immunity, morbidity, or mortality within the exposed population; (3) the balance in the proportion of the genes making up the body also may become the direct etiological agent of a definite pathological syndrome causing death or greatly reduced length of life; (4) during development the body, due to its inheritance, may become a mosaic of cells, some normal, some abnormal, and the morbidity and mortality increase directly with the proportion of defective cells in the mosaic.

Two thousand to fifteen thousand genes appear necessary to the development and functioning of an organism so small as the fly, Drosophila. A change of any one of these genes by mutation is lethal in more than 80 percent of the cases. The proper association of these genes in proper balance is necessary to the normal functioning of the vital processes.

Literature Cited

[1] Breasted, J. H., 1930, "The Edwin Smith Surgical Papyrus," Hieroglyphic transliteration, translation and commentary, Chicago University Presss, p. 596.

[2] Jones, W. H. S., transl. 1923, "Hippocrates," vol. i and ii, Loeb Classical Library, G. P. Putnam's Sons, New York.

[3] Mendel, G., 1865, "Versuche über Pflanzenhybriden," reprinted in *Flora: 89.*

[4] DeVries, Hugo, 1905, "Species and Varieties," Chicago, The Open Court Publishing Co., p. 847.

[5] Sutton, W. S., 1900, "The Spermatogonial Divisions in *Brachystola magna*," *Kansas Univ. Quart., 9,* 1902; "On the Morphology of the Chromosome Group in *Brachystola magna*," *Biol. Bull., 4:* 1.

[6] Cuénot, L., 1908, "Sur quelques anomalies apparentes des proportions mendeliennes," *Arch. Zool. Exp. et Gen., 4:* 9.

[7] Little, C. C., 1915, "The Inheritance of Black-eyed White Spotting in Mice," *Amer. Nat., 49:* 727-740.

[8] Detlefsen, J. A., 1923, "A Lethal Type in Mice, Which May Live for a Few Days After Birth," *Anat. Rec., 24:* 417.

[9] De Aberle, S. B., 1925, "Hereditary Anemia in Mice and Its Relation to Dominant Spotting," *Amer. Nat., 59:* 327-335.

[10] Gowen, John W. and E. H. Gay, 1932, "Physiological Factors Necessary to Alleviate Genetic Lethal Anemia in Mice," *Amer. Nat., 66:* 289-300.

[11] Nishikawa, H., 1931, "On Lethal Factors in the Silkworm, *Bombyx mori*," Sericultural Exp. Sta., Chosen.

[12] Crew, F. A. E., 1923, "The Significance of an Achondroplasia-like Condition Met With in Cattle," *Proc. Roy. Soc. B., 95:* 228-255.

[13] Mohr, Otto L., 1929, "Letalfaktoren bie Haustieren," *Zeit. Züchtungskunde, 4:* 105-125.

[14] Hadley, F. B. and L. J. Cole, 1928, "Inherited Epithelial Defects in Cattle," Res. *Bull. 86:* 1-35.

[15] Detlefson, J. A. and W. W. Yapp, 1920, "The Inheritance of Congenital Cataract in Cattle," *Amer. Nat., 54:* 277-280.

[16] Benedict, F. G., W. Landauer and E. L. Fox, 1932, "The Physiology of Normal and Frizzle Fowl, With Special Reference to the Basil Metabolism," Storrs Agric. Exp. Sta., *Bull., 177:* 13-101.

[17] Gowen, John W., unpublished.

[18] Biffen, R. H., 1905, "Mendel's Laws of Inheritance and Wheat Breeding," *Jour. Agric. Sci., 1:* 4-48.

[19] Walker, J. C., 1930, "Inheritance of Fusarium Resistance in Cabbage," *J. Agric. Research, 40:* 721-745.

[20] Gowen, John W. and R. G. Schott, 1933, "Genetic Predisposition to *Bacillus piliformis* Infection Among Mice," *Jour. Hygiene, 33:* 370-378.

[21] Rich, F. A., 1923, "Concerning Blood Complement," Vermont Agric. Exp. Sta., *Bull. 230:* 1-24.

[22] McRostie, G. P., 1921, "Inheritance of Disease Resistance in the Common Bean," *J. Amer. Agron., 13:* 15-32.

[23] Burkholder, W. H., 1923, "The Gamma Strain of *Colletotrichum lindemuthianum*," *Phytopath., 13:* 316-323.

[24] Bridges, C. B., 1921, "Triploid Intersexes in *Drosophila melanogaster*," *Science, 54:* 252-254.

[25] Gowen, John W., 1931, "On the Chromosome Balance as a Factor in Duration of Life," *J. Gen. Physiol., 14:* 447-461; "Metabolism as Related to Chromosome Structure and the Duration of Life," *J. Gen Physiol., 14:* 463-472.

[26] Reimer, F. C., 1925, "Blight Resistance in Pears and Characteristics of Pear Species and Stocks," Oregon Agric. Exp. Sta., *Bull. 214:* 1-99.

[27] Patterson, J. T., 1928, "The Effects of X-rays in Producing Mutations in the Somatic Cells of *Drosophila melanogaster*," *Science, 68:* 41-43.

[28] Gowen, John W., 1929, "On the Nature of Gene Action," *Science 70:* 358-360.

Gowen, John W. and E. H. Gay, 1933, "Gene Number, Kind, and Size in Drosophila," *Genetics, 18:* 1-31.

[29] Demerec, M., 1933, "Some Deficiencies as Cell Lethals in *Drosophila melanogaster*," *Rec. Genetics Soc. Amer., 2:* 57.

[30] Demerec, M., 1934, "The Gene and Its Rôle in Autogeny," Cold Spring Harbor Symposia on Quantitative Biology, vol. 2: 110-117.

The Government's Responsibilities in Science

(*Concluded from page 102*)

which are facing the country at those points at which science may offer hope of alleviation or solution.

Under these circumstances it seems to me certain that scientists will have to play an even more important rôle in the future than in the past. The problems to be solved are more complex, greater intelligence is needed in handling them, the scientific approach rather than the political or opportunistic approach is demanded. Whether directly in the government service, or indirectly in universities or industries of the country, there is no doubt but that men of the type found in the Society of Sigma Xi will find ample scope for their best efforts and in those efforts they will find careers of usefulness and of satisfaction.

PROGNOSIS*

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In inviting me to address you, our President stated that these exercises should be looked upon as part of Commencement and pointed out that it is the one part thereof in which the voice of the college proceeds at length. Such an invitation to proceed at length is not to be taken lightly and I presume that one should use it in the manner that most adults are expected to, namely, to give some words of advice and wisdom which you would carry with you for the rest of your days to help in avoiding some of the inevitable and horrific pitfalls of life. But after listening to a member of this student body, a short time ago, expounding the views of a really thoughtful student on the subject of advice, one hesitates about plunging into such a field. Still, apropos of that, and recalling that this is to be considered a part of Commencement, one may, at least, call attention to the fact that advice makes up an important part of our lives from beginning to end. Older folks give it and receive it about as much as younger ones give it and receive it. The chief difference appears to be that the older one becomes, the more readily does he receive it, listen to it, and welcome it.

It is dangerous to fortify such a statement as that above with an illustration which is exactly to the contrary, but nevertheless, I am reminded of the young man who had been in the employ of a certain company for a few weeks, then went to the president and complained of this and criticized that. After listening patiently for a time the president finally exploded and blurted out,

"Who do you think you are? Do you think you are the president of the company?"

"Why, of course not."

"Well, then stop talking like a fool."

Now there may be several reasons why we consider that incident amusing. But is not one of the reasons this, that we recognize it as so uncharacteristic of real men who hold positions of responsibility? They not only welcome, but they give the greatest consideration to, criticism and advice. They are literally hunting for it every day.

Well, so much for the subject of advice. I'm going to try to refrain from giving any today. And to change the subject suddenly: Has it ever occurred to you how many well-known objects and many familiar ideas appear strangely unsearchable when we look them in the face? That I am "I" to myself and "you" to all of you, who are each of you "I" to yourself is on contemplation, as has been pointed out by many a philosopher, a disturbing circumstance. That $2 \times 3 = 3 \times 2$ or $a + b = b + a$ appears so simple and axiomatic till it is subjected to analysis by the trained mathematician.

Were it not, as some one has pointed out, for our almost unlimited capacity for taking things for granted we should find ourselves encompassed by countless

* Annual Prize Day Address, Union College.

mysteries which might oppress our hearts beyond endurance did not custom and incuriosity veil the shallowness of our careless knowledge. Indeed, we must, at times, definitely shut ourselves away from too critical examination of the many incidents which come within our purview day by day, and moment by moment. Fortunately this is not difficult for most of us who are so inured to personality and to the banter of the marketplace that we, no doubt, err overmuch in that direction.

On the other hand, again, as has been pointed out, there have always been a few to whom these commonplaces have not seemed ordinary and who have looked beyond and beneath the surface. Through them our knowledge and vision of man, and the universe of which he is a part, have grown, from century to century. Roughly we may classify them as poets, religious leaders, moralists, story tellers, philosophers, artists, scientists, inventors. They are all discoverers and pointers-out. What eludes the attention of others catches theirs. They see where others are blind, and hear where others are deaf. They point out profundities, complexities, analogies, differences and dependencies, where everything had seemed as clear as a cloudless sky.

In the foregoing categories the group which we call scientists, has played an increasingly important part during the past 200 years and as a result of the so-called "scientific method" has contributed amazingly to almost every sphere of human thought and interest. So successful has this method been that many feel that statements regarding our environment or regarding man himself are of little value unless sanctioned by science. The term "scientific method" can be described in many different ways but one of its characteristics, it appears to me, has been its endeavor to carry on work in an impersonal way, independent of the observer. As though, in fact, man were not present in the universe. The attempt has been to dehumanize science and it has led to marked success. But of late the question has been arising more and more persistently as to whether our physical observations may not actually fail to represent reality; whether in spite of us they do not rather merely reflect personality, reflect the mind of man, giving back to us in tautological form the assumptions or axioms which we introduced at the beginning. Is there not a danger then, some say, that the dehumanizing process has gone too far and that it is time to rehumanize knowledge, or rehumanize science at least? Is it not possible that at least in the field of the study of man and the nature of man we have, in our concentration on certain viewpoints, been overlooking other equally important views? Does one really keep his feet on the ground when he tries, as do many scientists, to explain all phenomena regarding mankind on a materialistic or mechanistic basis?

It is peculiarly this question of man and what he is going towards, if he is going towards anything, that should engage the attention of a body of thoughtful students and I would therefore address myself to it this morning. It is with a considerable feeling of diffidence that I do so because from a scientific point of view this is especially the field in which the biologist and the psychologist are supposed to speak with the voice of authority. On the other hand it is one of those questions that affects so intimately the philosophy of life which

each one of us must formulate for himself. That philosophy may be a formulation based on careful study and long thought, or, it may be based solely on our objective contacts with life integrated over the number of days we have lived and the ordinary experiences crowded into them. The fact that in the latter case it has not been a conscious building of a philosophy does not make it any less important, at least to the individual concerned who must conduct his life in accordance with it. It is the kind of question on which each of us feels entitled to an opinion just as each of us feels entitled to, in fact must have, opinions on money matters although we may not be bankers; or on social proprieties although we may never have read Emily Post.

Well! it is on this basis then of being neither a biologist nor a psychologist but merely a physicist and yet having certain views, that still I venture to approach the subject of the future of mankind, risking the charge of immaturity or superficiality.

Recently one of my esteemed colleagues speaking here on the subject of Progress gave it as his opinion, if I understood correctly, that the human race has not changed for an immeasurable time in the past and would not change in the future. That life for the human race consists in generation following generation with no intrinsic change in physical or intellectual capacity, but solely with an accumulation of knowledge stored up in books or elsewhere which may, perhaps, lead succeeding generations to act, not with more wisdom or intelligence but merely with more discretion because of more information at hand. In other words, human nature does not change.

Now I am aware that there are many scientists, psychologists and others, who agree with this view but, if I read correctly, there are also many who do not. To me, it is a frankly discouraging and even depressing outlook, "as cold as blasted hope." To many it seems to take away much of the objective and joy of life and makes it cheap. It tends towards a cynicism on the part of some which is anything but healthful as for instance when, in moments of pessimism, they say, "Well! human nature never changes."

Can we find that their outlook is really justifiable; justifiable on a scientific basis, using such scientific information as we possess today? I should like to bring to you or remind you of some of that information. For that we can, of course, look only to the past and add to it a little of recent experimentation and recent speculation. But, "very deep is the well of the past. Shall we not call it bottomless? Bottomless indeed, if the past we mean is the past merely of the life of mankind, that riddling essence of which our own normal unsatisfied existences form a part; whose mystery, of course, includes our own, and is the Alpha and Omega of all of our questions, lending burning immediacy to all we say and significance to all our strivings. For the deeper we sound, the further down into the lower world of the past we probe and press, the more do we find that the earliest foundations of humanity, its history and culture reveal themselves unfathomable. No matter to what hazardous lengths we let out our line they still withdraw again, and further into the depths. Again and further are the right words, for the unresearchable plays, a kind of mocking game with our researching ardours; it offers apparent holds and goals behind which,

when we have gained them, new reaches of the past still open out—as happens to the coastwise voyager who finds no end to his journey, for behind each headland and clayey dune he conquers, fresh headlands and new distances lure him on."

Nevertheless, and in spite of the lack of finality, on the basis of science, the matter of evolution comes in. Not that we will argue on whether man ascended from the monkey or descended from the angels, but rather we will make the statement that the principle of evolution is accepted by all. I shall assume that it is. But, to me, the thought of evolution carries with it the idea of change, for better or worse, of movement, forward or backward. Is the human race free from this? Surely it developed either by perceptibly large or imperceptibly small steps, by one method or another, from something different from what it is now and we have strong evidence that it has been in the direction of what we call "progress," an increase in intellectual power, artistic sense, moral consciousness. Is there any reason to believe this has stopped and if so, why and when?

It may be that the marked difference of expression is due to the magnitude of the time elements which are being considered. It may be, for example, that when people speak of human nature not changing, they have in mind a period of some three or four generations. But obviously, this is entirely too short a time from which to draw any conclusions. I should say that the shortest time which need be considered is a matter of one or two thousand years, for let us bear in mind that the 2,000 years of the Christian era, which seems so long, amounts to only about sixty generations; and sixty generations in the evolutionary history of any living organism is a comparatively short time. Still we hear it said with considerable dogmatism that the human race has not changed in ten or twenty thousand years and much less so in two thousand years.

Now I seriously question the basis for such statements, for what do we actually know of the intimate thoughts and intimate life and intimate perspicacity of any particular group of people of 2,000 years ago? Do we know them well enough so that we can, with confidence, say that they are superior or less superior than ourselves in this field or that field? So far as I can see there are no standards of comparison which are absolute and on which we can rely, even in the matter of three or four generations. Who of us has not frequently wondered what the real thoughts and outlooks were of our own race so recently as 100 years ago and how eagerly we question a person of the ripe age of eighty or ninety to learn what people were really like in his early years. And how inconclusive and unsatisfactory their answers are as applied to the question we have in mind. If that is the situation now, what must it be when we talk of people of 2,000 years ago; and still more, when we talk of the human beings of 10,000 or 100,000 years ago? Interesting and important as are the historical records which we have of the people of 2,000 years ago, how meager they are after all, and when it comes to those of the longer period, we apparently have little else but a few parts of skull bones, some teeth, an occasional thigh bone, and some implements, from which to draw conclusions. I would submit, then, that all of our records are entirely too meager to serve as a basis for a

categorical statement that the human race has not changed appreciably in its intimate thoughts and in its mental capacity in any period so short as 10,000 years.

On the contrary, the teachings of evolution would lead us to believe that the human race is not any more static than any other form of life. In this connection I would quote Dr. Hrdlicka of the Smithsonian Institute, when, in speaking of evolution, he says, "There is no indication that there will be any perceptible retardation in mental progress and physical evolution of civilized man during the next few thousand years. Man is still as plastic in body and mind as he ever was, probably more so; he is still struggling with environment, though controlling it more and more every day; and he still changes."

To me, this point of view is an important one. It is encouraging and, at least until I am compelled by evidence to accept another view, I should prefer as a general policy to adopt that one by which to govern my life, which is the more hopeful and optimistic.

Personally, I like to think of evolution as not merely a process but a broadly continuing process, starting from some elementary form of life and coming up to an important stage when, for some reason or other there developed, shall we say in a turtle, the beginnings of a cortex in the brain. This particular phenomenon of the land turtle which has a cortex and the water turtle which does not, is one which has been most fascinatingly described by Dr. W. R. Whitney, one of the trustees of Union College, in an address which he gave before the Union chapter of Sigma Xi just a year ago and I would commend it to you.[1]

From this beginning of a cortex there has continued an extended and amazing evolution up to the present stage in mankind which, in all modesty, we take to be the highest development found in any form of animal life. Can we believe it has stopped? If so, why? Has nature exhausted the effectiveness of her past methods and has she no novelty for the future? Is it not much more justifiable to believe that evolution and change are to continue in the human race?

I trust that these remarks do not lead to the impression that I am ignoring the significance of the constancy of human nature. Quite the contrary. I would agree that it is nearly unchangeable but not quite. It is that degree of unchangeableness, call it heredity if you wish, which is the source of stability and strength of the human race, which keeps it from fluttering around in response to every current and eddy, good or bad, like a weather cock. It is the very salvation of the human race. Let us not fail to recognize that each new generation must start at about the same place as the previous generation, but for our purpose it is sufficient and very precious if that new generation can start only slightly ahead and go only slightly further, for then the cumulative effects over a long period of time, become of controlling importance.

And may not this be the answer to the statement so frequently made, that Christianity has been a failure? Who of us has not heard the man who in one breath says: "Human nature does not change," and in the next, "Christianity is a failure because in 2,000 years it has not produced a spiritually perfect race

[1] SIGMA XI QUARTERLY, September, 1934.

in accordance with the teachings of Christianity." If the child of one generation could start on a level of spiritual and moral consciousness and understanding, where his parents were at the time of his birth, then Christianity would indeed be a failure for not having produced a better race in these directions. But, each generation must start from at least nearly the same place, and again I would say it is sufficient and very precious if each generation can start only slightly ahead and go only slightly further than its immediate forebears.

It is with this in mind, as one looks for changes in the physical or intellectual capacities, or the spiritual life of a group of the human race, that the two thousand years of the Christian era, to which we referred above, is seen in better perspective.

Now to change the scene. Something more than a century ago the French mathematician, Laplace, stated quite definitely an idea which had been gaining ground in the minds of many and which we may call the principle of determinism. His statement I quote as follows:

> "We ought then to regard the present state of the universe as the effect of its antecedent state and the cause of the state that is to follow. An intelligence, who for a given instant should be acquainted with all the forces by which Nature is animated and with the several positions of the entities composing it, if further his intellect were vast enough to submit those data to analysis, would include in one and the same formula the movements of the largest bodies in the universe and those of the lightest atom. Nothing would be uncertain for him; the future as well as the past would be present to his eyes. The human mind in the perfection it has been able to give to astronomy affords a feeble outline of such an intelligence. . . . All its efforts in the search for truth tend to approximate without limit to the intelligence we have just imagined."

According to this principle, the future of every piece of matter, organic and inorganic, vital and non-vital, is clearly and definitely preordained, the situation throughout the universe for large bodies and small being at any moment precisely determined by the circumstances immediately preceding, and they, in turn by those immediately preceding. Thus the whole future as well as the whole past of the universe would be perfectly clear to and predictable by a sufficiently powerful mind. Every act of every individual is preordained.

Now this principle grew up as a result of the discoveries and formulation of laws in the most materialistic of the sciences, namely the field of what we now call "Physics." But the principle has permeated all lines of thought, scientific and otherwise, and has been very powerful in its influence. In the field of religion, for instance, it has played an important part under the name of "pre-destination." Under it there seems to be no room for mysticism in art or religion or life. "Nature or God is simply turning over the pages of a story written eons ago or cranking a mechanism to make stars and planets move in predetermined ways and human puppets to dance on the earth." To be sure, there were many who, although unable to disprove the principle, were unwilling to accept it because of its repellent implications, especially in the field of personality and the spiritual life. But a dyed-in-the-wool scientist

could not well avoid it. Some endeavored to overcome the difficulty in their own minds by saying that the principle of determinism undoubtedly holds in the inorganic world but that in the field of living organisms, especially in the human race, there was some principle which was not subject thereto and which left room for the play of free will. They were in a very difficult position, for they rather had to believe that a man can think what he likes but can move his lips to say only that which the laws of physics preordain.

Beginning about the middle of the last century there was developed a branch of science known as thermo-dynamics in which the theory of probability came to play an increasing part until it encompassed the whole field and we now recognize that that important field is nothing much but a matter of probabilities. It became increasingly evident that in some fields, at least, there were no certainties or laws of certainty but that if one were dealing with a large number of particles, the laws of averages and probabilities indicated a very high likelihood but not a certainty of an event occurring.

In spite of these developments I think it is fair to say that up to ten years ago every physicist of repute was, or believed himself to be, a determinist, at any rate as far as inorganic phenomena are concerned. But about that time Heisenberg of Germany, pointed out, as a consequence of the Quantum Theory, that there is an inescapable uncertainty in any measurement of physical quantities and stated this under what is known as the Principle of Indeterminacy or Uncertainty. We know it now to be related to that uncertainty already recognized in the field of thermo-dynamics. Let it be clear that in speaking of this "uncertainty" we are not referring to imperfections in our apparatus or in our powers of observation but to something far more subtle and fundamental.

Perhaps I can illustrate this best by a concrete example. In studying the mechanics of any body the quantities we usually desire to measure are position and velocity. It develops that we can determine the position of an electron with as high accuracy as we wish but in that event we know less and less about its velocity, or we may measure its velocity with high accuracy, but only by sacrificing knowledge as to its position. If, for example, we desire to know the position of an electron to .01 millimeter we cannot by any possibility find its velocity more accurately than within about 100 meters or 300 feet per second. If we are satisfied to know the position to within 1 millimeter then we can, with "perfect" instruments, find the velocity to an accuracy of about 1 meter per second. The more accurately we determine one quantity the less accurately can we determine the other. We can divide the inaccuracy as we desire but we can never get rid of it, we can never reduce it below a definite quantity the value of which is related to a well-known constant of nature, called "Planck's Constant."

We can see better why this is so if we note that in order to locate the position of an electron we must make some observation on it. We might, for example, look at it with a highly ideal and powerful microscope. But such an observation would be possible only by reflecting light from the electron and in the very process of reflecting the light into the microscope for us the electron is itself deflected by an unknown amount which thus renders its exact

position uncertain. Any and every other observational measurement we have been able to conceive turns out to be subject to an analogous uncertainty.

If we deal with large bodies instead of small ones the uncertainty becomes relatively less important because of the size of the quantities which we are measuring but it is still present and somewhat larger, for the behavior is the aggregate of that of the molecules of which it is made. Because of, and within the limits of this uncertainty, it is impossible for any mind, however powerful, to tell what will happen even though he has the initial data which Laplace assumed. It would be impossible to predict the future with anything more than a comparatively high degree of probability. Even in the motion of astronomical bodies, the positions of which we have come to feel and know by experience that we can predict with a high degree of accuracy, we now know we cannot make determinations with absolute certainty. The likelihood of departure from our calculated prediction may be exceedingly small but nevertheless is present.

Now every physicist and philosopher who has considered this principle recognizes that former laws, which we thought to be deterministic are not so but appeared to be so only because our measurements were not sufficiently precise to note the departures. Our point of view in this respect has had to be radically changed, and this new outlook has been a great awakening. It has given an entirely different appearance to the universe. As Hermann Weyl, the well-known relativity mathematician has said: "We must await the further development of science, perhaps for centuries before we can design a true and detailed picture of the interwoven texture of Matter, Life, and Soul. But the old classical determinism of Laplace need not oppress us any longer." Predestination and preordination are dead. And let it be emphasized that this rejection of determinism is in no sense an abdication of the scientific method. Quite the contrary, it is a fruition thereof. It is not, as some have facetiously remarked, a case of going off the gold standard.

I wish I might discuss further the details of this Principle of Indeterminacy, just as a matter of physics, but the brief time at our disposal does not permit. I would ask you to accept it and to look into it because it will undoubtedly play a great part in our future outlook on life.

Now a question of interest to us is, whether this principle of indeterminacy is applicable to those aspects of life which we call the intellectual, spiritual, and moral aspects. It is true that the greatest caution should be used in applying the principle to other than the field of non-vital matter. And just as there were some, who, in earlier days admitted determination as far as non-vital matter is concerned, but hesitated about applying it to living or conscious matter or to consciousness itself, so there will be some now in this new period who will admit the principle of indeterminacy as far as non-vital matter is concerned, but will doubt its application to life. Scientists have been considering the question profoundly and with caution but the drift of thought has been definitely toward acceptance of its application in all things relating to the universe. The fact that it must be so is excellently set forth by Sir Arthur Eddington, in his recent book, "New Pathways in Science."

The profound nature of such application is apparent to all, when it is recognized that this may mean the reintroduction and acceptance of the possibility of free will, which for 200 years has been denied by the scientific world, and been highly debated in the field of philosophy.

But the important point, for us this morning, is the fact that if the principle is applicable it is impossible to predict what the future of the human race may be. While it would be as crassly unintelligent to ignore history as it would be to now ignore the so-called laws of physics, still, having made a prediction based on history, we would have to recognize that the trend of human nature may depart, at first slightly but later very far from that prediction. The future is never entirely detached from the past, but neither is it ever entirely determined by it.

The point may be made that as an aggregation of molecules, the uncertainty associated with a chunk of matter as large as a human individual is so small as to be entirely negligible and that the same would be applicable to that which we call personality or ego. If personality or ego is, indeed, made up of as many individual things or particles equivalent to molecules, as is the physical body then this contention may be justified. But again, as Sir Arthur points out, there is no reason to believe that personality can be divided into parts. It is more probable that personality must be looked upon as a single entity such as a single atom or electron; and as I read the present trend in psychology, it appears to me that psychologists are coming to look on the ego as a unit and not as an aggregation of small entities. If it is of unitary nature it is presumably subject to indeterminacy of behavior as great, relatively, as for a molecule or electron.

Now I refer to all this rather abstruse matter not so much for the purpose of expounding the principle of indeterminacy with its implications of free will, but rather to point out the fallacy of relying any longer, because of its alleged position in physics, on the principle of determinism in any field of human interest and the grave danger of theorizing on its basis.

Formerly many have had to base any belief in a rising mankind on faith and if it comes to faith there is about as much room to believe one thing as another. In that event I would prefer to take the more beautiful and optimistic one. Now, however, with what seems to some a return to freedom of will in its higher sense and nothing to deny an indefinite evolution, there is a lifting of a burden from the mind and the heart which gives renewed hope.

Well! at this stage I'm reminded of the darkey preacher who was asked how he prepared his sermon. He said: "I divides my sermon into three parts: first I tells 'em what I is gwine to talk about, den I tells 'em, and den I tells 'em what I is done told 'em." A polite way for the last part is to say: "And now to summarize." That statement will be received with satisfaction for it is a promise of an early termination, perhaps we should say, "a high probability" but it is not a certainty and I suspect before I am done that you may conclude the uncertainty was higher than you had thought possible.

But to summarize:

1. On the basis of evolution I am unable to see how or why we should assume the human race has reached a static condition.

2. The evidence seems to be that the human race is flexible and is changing. It may be nearly constant but not quite.

3. No part of the universe, including mankind, need any longer be looked upon as subject to the laws of determinism.

4. It is difficult to see how personality or ego can be placed outside the principle of indeterminacy.

5. This would seem to restore freedom of will and put back into life that mystery which science was said to have removed some decades ago.

Now one more thing to bring into the picture. In my quotation from Hrdlicka he said, man is still struggling with environment and controlling it more and more every day. The rate of increase of control has been phenomenal during the past 200 years and especially during the past few decades, chiefly due to what we call the "scientific method." As a result of this we are living in a great epoch, as great as that of Copernicus which led to the overthrow of the geocentric outlook. This present epoch is extraordinary in the rapidity with which new conceptions are being introduced and the profound influence of these conceptions on human life and conduct. And most important of all, it seems to me that there has come and is coming the idea that man himself has the ultimate ability to control for his own ends many of the changes going on in this world.

Today, as a result of the work in the pure sciences, the following out of the desire to know, we live in an epoch of two ideas. One is that of the possibility of continuous progress. The other is that of man's ability to control and determine to a large extent his own destiny, the idea of his own responsibility for the kind of external world in which he lives. We have been forming the habit of looking on everything as not finished but as in the process of becoming. We do not know what man is to become and there is much we do not know of him as he now is, but he is a creature of whom we may say that our knowledge is helpfully good and hopefully incomplete.

And what is our part in this? The tendency of people is to listen to such ideas but to assume that they will take care of themselves or that others in more important places will do something about it. On the contrary this idea of controlling our destiny, *i.e.,* shaping the evolution of the race, is dependent on the actions of large numbers. And to the extent that large numbers are imbued with the same idea, and consciously so, the change will be the more substantial.

I say change, for it may be either progress or retrogression. It is not inevitable that evolution shall be towards betterment. The doctrine "Let yourself go," so commonly preached during what Doctor Canby, speaking here recently, called the "Decade of Youth" can lead to nothing but catastrophe. On the contrary the doctrine of self-control and self-responsibility is the only one which can assure that the change will be one of progress.

Each in his own way, by his life and his character contributes for well or ill to the sum total of advance or retrogression. And what an interest, what a zest it adds to life to know that, to such extent as we may wish, we are a

(*Please turn to page 134*)

SOME RECENT ADVANCES IN CANCER RESEARCH*

C. C. Little

Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine

We may preface our discussion of some of the more recent advances in cancer research by a very brief definition of cancer which was given in 1916, as follows:

> "Biologically, cancer may be considered as consisting of a mass of tissue of local origin manifesting uncontrolled and unlimited growth. The problems of its etiology are, therefore, essentially those of the factors causing, limiting and directing cell division."

It is, in a way, unfortunate that everyone uses such a term as "cancer" to describe this phenomenon. The term indicates nothing whatever to help us bear in mind the fundamental characteristics of the phenomenon which we are studying.

In spite of the somewhat childlike psychological processes involved, there is real value in using terms which help us to keep constantly in mind the nature of a process which we are trying to explain or to analyze.

Last year, therefore, at the fiftieth anniversary celebration of the Memorial Hospital in New York the suggestion was made that the phrase "hypernomic histoplasia" be employed in place of the term "cancer."

The term "histoplasia" is in good use both medically and biologically. Tissue formation is a characteristic of all tumors—both benign and malignant. Its inclusion in any descriptive phrase is therefore essential. "Hypernomic" is a less frequently employed, but equally well sanctioned, word denoting "outside the law" or "above the law, in the direction of assertive action." It exactly describes the definitive character of cancerous growth as distinguished from that of benign tumors, or of orderly tissue formation during ontogeny.

In biological research therefore we are studying the factors that cause or allow "hypernomic histoplasia"—the formation of tissue, outside the law of orderly ontogenetic processes or of growth control, which commonly characterizes that series of events.

THE NATURE OF MAMMALIAN INDIVIDUALITY

Since the process of hypernomic histoplasia involves a reaction by, and utilization of, the actual tissues of the animal itself rather than the introduction of a foreign body, a brief statement concerning our present conception of mammalian individuality may be helpful.

The ages characterized by the most effective expression of well-integrated physiological individuality are those most free from signs of any insurgent local growth process of any kind. This period may be looked upon as that with the most clear manifestation of centralized control—a control gradually acquired during adolescence and lost again during senility.

* Address at Sigma Xi initiation, Brown University.

The importance of this fact has been somewhat underemphasized in our conception of the nature of the mammalian individual. It is necessary to keep it constantly in mind if we desire to analyze, in even an elementary way, the conditions under which hypernomic histoplasia occurs—and so derive a clearer conception of its meaning.

A measurement of the degree to which centralized control of any single physiological process is effective, is the extent of variation in the expression of that process, within animals of similar genetic constitution, kept under as nearly as possible constant environmental conditions.

Preliminary data on litter size in mice and on the amount of crossing over in Drosophila were presented in a brief note in *Science* in 1933. Later experiments continue to offer evidence in support of the conclusions then reported. Certain of these may, therefore, be profitably repeated, as this time, as follows:

> "1. 'Individuality' in mammals and probably in all higher animals, is a relative term with a well-pronounced durational phase.
>
> "2. Within genetically comparable material, variability in form and function is greater in the very young and in the very old animal than it is in those which are in the height of reproductive efficiency.
>
> "3. Measurements of simple increase or decrease in function are not sufficient to give a complete picture of the nature of individuality. A measurement of *variability* is required.
>
> "4. Senility is not simply a 'major involution' but rather a period at which the disintegration of individuality is the most interesting and important biological phenomenon. . . . ."

To supplement these facts we know that the distribution of hypernomic histoplasia bears a very clear and striking relationship to the age of the individual. Without taking time to discuss this matter in detail, it may be stated that adolescent or old individuals are more apt to form tumors than are those *in the height of their reproductive activity*. This is generally recognized in both laboratory mammals and in man.

Expressed in terms of our conclusions as to the nature of individuality, this means that hypernomic histoplasia occurs chiefly at those periods of the development of the individual when centralized control is weakest and variation in the expression of the animal's physiological and morphological characteristics is greatest.

Since hypernomic histoplasia *accompanies* manifestations denoting a weakening of centralized control, it is the simplest working hypothesis to assume, that light on the origin of hypernomic histoplasia will be obtained by increased knowledge of the factors that cause and accompany this decrease in integration and effective organization of the individual. Some of these may next be considered.

There are two groups of factors which contribute to the appearance of tumors. The first of these includes what may be called the histogenous factors; the second is comprised of the irritational or stimulative factors. In the first group, it is obvious that only the actual nature of the tissue itself can be concerned; in the second, the irritants may be either external, internal, or both in

origin. It is also clear that, no matter what the origin of an irritant may be, its effect must have become internal in nature before the substance of the cell reacts in such a way as to free it from controlling agents. The relationships between the two types of factors are undoubtedly complex. This makes it very difficult to distinguish them from one another or to evaluate properly and accurately their relative importance.

A beginning in this direction has, however, been made and can be briefly discussed at this time.

It has been recognized for some years that different inbred strains of mice exhibit characteristic and widely divergent degrees of tendency towards hypernomic histoplasia. This fact rests on a firm foundation of experimental results obtained by Tyzzer, J. A. Murray, Loeb, Slye, Lynch, Zavadskaia and others. None of these investigators, however, continued rigid and close inbreeding of their various foundation stocks to a point where genetic uniformity was obtained. As a result, the outcrosses made by them between strains supposedly high in hypernomic histoplasia and those low in this process, lacked accuracy and definiteness. The completion of routine inbreeding, continued over a long period of time, is the result of a dull and uninspiring process. It delays the opportunity to make interesting outcrosses and thereby postpones the more important and significant results. It cannot, however, be safely omitted if we are to obtain predictable results which are capable of repetition.

For this reason, it has seemed wise to devote a period of years to preparatory and preliminary work in the genetic purification and simplification of strains. In 1930 a number of inbred strains had reached a point approaching theoretical homogeneity sufficient to allow their use for outcrosses.

Focussing attention particularly on tumors of the mammary glands—the commonest type of neoplasm in mice—several outcrosses between "high" and "low" strains were made.

We may especially consider the one of these in which the difference between the parent strains was greatest and the number of progeny obtained was the largest.

The strain, high in tumors of the mammary gland was dilute brown in color. It is designated by the symbols dba. The other parent strain, in over fifty generations has given no instance of a malignant tumor of the mammary gland. It is black in color and is designated as C57.

Since malignant tumors of the mammary gland have never appeared in male mice of either strain *females* alone were used in calculating the incident of this type of neoplasm. The experiment was carried out cooperatively by Dr. W. S. Murray and the speaker.

Since, also, pregnancy and lactation have an influence on the incidence of tumors of the mammary gland, virgin females were used for tabulation. To produce an F_2 generation, sisters of the virgin F_1 females were employed.

The outcross was made in two ways—as follows:

(a) dba ♀ x C57 ♂
(b) C57 ♀ x dba ♂

The F_1 results were:

(a') 113 ♀s 45 or 39.8% with hypernomic histoplasia of the mammary gland.

(b') 356 ♀s 23 or 6.46% with hypernomic histoplasia of the mammary gland.

The difference is approximately sixteen times its probable error.

This result is unique and important. It shows conclusively that, while the genetic (*i.e.*, chromosomal) constitution of the two groups of virgin F_1 females is identical, the amount of tumor formation in the mammary gland shown by them differs widely. There is therefore some sort of extra-chromosomal influence present and operative in producing the difference.

That this influence also affects the two types of F_2 females is proven by the following results:

F_2 ♀s derived from

(a') 664 of which 236 or 35.54% show hypernomic histoplasia of mammary gland.

(b') 687 of which 41 or 5.96% show hypernomic histoplasia of mammary gland.

The two reciprocal F_2s differ widely from one another but resemble, in each case, their respective F_1s, very closely.

This definitely indicates that the major influence on the formation of tumors of the mammary gland in mice is transmitted to a far greater degree through the female than through the male. Experiments are now under way to investigate this matter more completely with the purpose

(1) of separating more clearly the chromosomal and non-chromosomal influence

(2) of determining, if possible, whether the non-chromosomal influence is carried in the cytoplasm of the egg.

In this way, then, slowly, and it must be admitted, a bit clumsily we are trying to analyze some of the histogenous factors involved in the process of hypernomic histoplasia.

Another interesting and probably significant fact is the age at which different general types of hypernomic histoplasia occur.

In humans the peak of incidence of mammary tumors is in the neighborhood of the fiftieth year. On the other hand, the mode of the age distribution of malignant tumors of the digestive system is at a point approximately ten years later. Statistical data are never very satisfactory in a study of human material and are mentioned here merely to show a general trend.

In mice, however, the evidence is very clear that the vast majority of cases of tumors inside the peritoneum, occur at a much later age than do those in the mammary glands. This fact has, of course, been taken into consideration in the analysis of the material just presented.

There remains, however, the main point of the age difference of the two groups to be explained.

The simplest working hypothesis, and one which is now being tested is that the incidence of hypernomic histoplasia is, in some intimate way, connected with the differential rate at which centralized control of various tissue systems is

(a) attained in young animals
(b) lost in old animals.

In these two groups, the process is much more characteristic of old animals than of young.

It seems probable that hypernomic histoplasia is the result of interaction between a cell and its internal environment.

If in a normal female animal the reproductive system is among the first to reach a stage of disintegration one would expect the situation to be favorable to hypernomic histoplasia—as it actually is.

There are several pieces of work by Murray and others that bear on this point. One has already been mentioned. It is that in virgin females the incidence of tumors of the mammary gland is less than in breeding females. It is also true that the actual mass of mammary tissue in virgins is less. It is not subjected to the cyclic changes of pregnancy or lactation. It probably wears out more slowly and with less chance of the production of critical physiological complications.

Male mice possess mammary glands which are rudimentary—their development having ceased at the fifth day, postpartum. They do not develop hypernomic histoplasia of the mammary gland.

Murray showed in 1927 that certain castrated males, in which the ovary of a sister mouse had been transplanted, would maintain and feed the transplanted ovary. In these mice the mammary tissue is histologically similar to that of virgin females. So also is their incidence of tumors in that region.

Lacassagne repeated the experiment using injections of theelin instead of a transplanted ovary and obtained similar results.

As a supplementary study, Murray removed the ovaries from breeding female mice just before they reached an age at which they might otherwise be expected to show hypernomic histoplasia of the mammary gland. This process both actually decreased the incidence of tumors and, in those animals which exhibited them, delayed their appearance significantly.

This tends to show that two factors are at work. One is the amount of mammary tissue which the animal possesses. There is some positive correlation between this and the amount of hypernomic histoplasia in that tissue. The second is the stimulative effect of ovarian secretion such as theelin. There appears to be some direct effect of this secretion on the mammary tissue. Neither of these factors can be effective unless the histogenous factors of a given animal are such as to encourage the appearance of hypernomic histoplasia.

We may diagram the situation as follows:

Hypernomic histoplasia

↑

III	Attainment of certain degree of "age" of gland	Usually made more rapid by ovarian activity
II	Formation of a necessary minimum of mammary tissue	Dependent upon a certain amount of ovarian hormone
I	Constitutional and transmitted factors	Transmitted about 6x as much by influences outside the chromosome as by those within it

We do not yet know whether the constitutional and transmitted factors which show such marked evidence of extra-chromosomal influence are operative in many non-mammary types of hypernomic histoplasia.

The definite organ localization of hypernomic histoplasia in certain strains indicates that, even if general tendencies to show this phenomenon are being transmitted, modifying agents, of one sort or another, are undoubtedly at work. These tend to limit or define the regions of the body, or the tissue or organ systems in which the tendency will express itself.

There remains for consideration many interesting topics. The necessary limitations of your patience and of our time, preclude most of these. One, however, deserves a little attention. This is the nature of the change from normal cells to those contributing to the hypernomic histoplasia.

Tyzzer, some nineteen years ago, suggested that the change in question might be in the nature of a mutation. At that time we knew little of the various types of germ cell reorganization that have since been studied.

A whole group of investigators showed that variation, which fulfilled the requirements of being both sudden and self-perpetuating, could be produced by duplication of individual chromosomes or by whole sets of these bodies. The work of Blakeslee and his associates is outstanding in this field.

Others, notably Muller, showed that *intra*-chromosomal changes of either a gene or a small area of the chromosome also produced mutations.

X-rays and certain other agents increase the incidence of such mutations. They also tend, in some cases, to lead to the appearance of hypernomic histoplasia.

The faithful transmission of the hypernomic quality from one cell generation to another for an indefinite period, meets the definition of a mutational change.

The sporadic occurrence of areas of hypernomic histoplasia in occasional animals of inbred stocks where no such tendency is regularly expressed, is also indicative of a process akin to or identical with mutation.

If, however, the mutation of somatic issue is the explanation for the occurrence of hypernomic histoplasia it is still necessary to determine why certain strains

of animals produce this change regularly in as high as 85 to 100 percent while in others it is absent.

By accepting somatic mutation as a working hypothesis, therefore, we have not solved the major problem which remains unaffected by the hypothesis under discussion.

The mutation, if such it is, evidently does not, primarily, affect the distribution of whole chromosomes. Even though Boveri's theory in this respect, still has its supporters it is weaker at present than it was when first offered. Many tumor cells *have* abnormal numbers of chromosomes both in excess and less than the normal quota. Such cells, however, are, in comparison with those having the normal number, weak and inactive. The excess of mitotic activity which is the very essence of histoplasia is largely confined to those cells with the normal chromosome count.

The advances already made since a genetic and biological approach to the cancer problem has been organized are encouraging. The increasing interest in the problem and its inclusion in the programs of more and more research laboratories augur well for the future. Little by little we are making headway. The progress made indicates that increased knowledge of the nature of mammalian individuality, and of the interrelationship between genetics and physiology in their contribution to the nature of the organism, is opening up a new and fascinating field in which the need of more workers is certain to be great—for years to come.

Prognosis

(*Concluded from page 127*)

part of that movement, so that we may indeed join with the poet when he sings:

"Lord of creation, we give thee thanks
That this Thy world is incomplete;
That battle calls our marshalled ranks,
That work awaits our hands and feet.

That Thou hast not yet finished man,
That we are in the making still,
As friends who share the Maker's plan,
As sons who know the Father's will.

Since what we choose is what we are,
And what we love we yet shall be,
The goal may ever shine afar;
But the will to win it makes us free."

REPORT OF COMMITTEE OF AWARD OF SIGMA XI GRANTS-IN-AID
FOR 1935-36

The Committee of Award of Sigma Xi Grants-in-Aid met in August at Harvard University and made the following grants for the academic year 1935-36:

PROFESSOR LEONARD B. CLARK, Union College, $250. *Project:* Recovery process in amoeba after stimulation by light. *Sponsors:* Dr. Selig Hecht, Columbia University; Dr. S. O. Mast, Johns Hopkins University Dr. H. S. Jennings, Johns Hopkins University; Dr. William L. Dolley, Jr., University of Buffalo.

PROFESSOR NEPHI WILLARD CUMMINGS, San Bernardino Valley Junior College, California, $100. *Project:* Further calibration of the Burt phototube as a pyrheliometer; further studies with the thermally insulated evaporation pan in the hope of developing methods for obtaining automatic records; the relation between transpiration and evaporation from soil on the one hand and insolation and atmospheric conditions on the other. *Sponsors:* Dr. Robert A. Millikan, California Institute of Technology; Mr. F. C. Ebert, Senior Hydraulic Engineer, United States Geological Survey; Mr. Geo. F. McEwen, Scripps Institute of Oceanography, University of California.

PROFESSOR ERNEST EDWARD DALE, Union College, $100. *Project:* Inheritance of variegation in Salpiglossis. *Sponsors:* Dr. L. W. Sharp, Cornell University; Dr. E. G. Anderson, California Institute of Technology; Dr. Frieda C. Blanchard, University of Michigan.

PROFESSOR W. J. LUYTEN, University of Minnesota, $100. *Project:* Proper motion of stars. *Sponsor:* Harlow Shapley, Harvard University.

DOCTOR FREDERIC COWLES SCHMIDT, Union College, $50. *Project:* Study of heats of reaction in liquid ammonia. *Sponsors:* Dr. Charles A. Kraus, Brown University; Dr. Earl K. Strachan, Brown University; Dr. Edward Ellery, Union College.

DOCTOR FREDERIC A. SCOTT, Lehigh University, $300. *Project:* Study of positron spectrum of the thorium active deposit; redetermination of end-point of B-ray spectrum of radium E. *Sponsors:* Prof. H. A. Wilson, Rice Institute; Dean F. K. Richtmyer, Cornell University; Prof. C. C. Bidwell, Lehigh University.

PROFESSOR THOMAS LATHAM SMITH, College of the Ozarks, $100. *Project:* Continuation of the experimental work on the genetics of the wax moth, including an attempt to analyze the cause for sterility between two strains of the same species of the moths. *Sponsors:* Prof. D. E. Lancefield, Columbia University; Prof. J. H. McGreggor, Columbia University; Prof. G. N. Calkins, Columbia University; Dr. Wiley Lin Hurie, College of the Ozarks.

DOCTOR DUNCAN STEWART, JR., Michigan State College, $200. *Project:* Continuation of a petrographical study by modern quantitative methods of rock

specimens from Antarctica. *Sponsors:* Prof. Laurence M. Gould, Carleton College; Prof. Walter F. Hunt, University of Michigan; Prof. Wm. S. Hobbs, University of Michigan.

PROFESSOR CHARLES OSCAR SWANSON and PROFESSOR JOHN HUNTINGTON PARKER, Kansas State College, $100. *Project:* Study of the inheritance of gluten strength in wheat hybrids, as determined by the wheat-meal-time fermentation test. *Sponsors:* L. E. Call, Director, Kansas Agricultural Experiment Station; R. I. Throckmorton, Head, Department of Agronomy, Kansas State College; Dr. E. G. Bayfield, Ohio Agricultural Experiment Station.

PROFESSOR EVERETT WHITING THATCHER, Union College, $400. *Project:* Study of multiple space charge. In particular, its influence on statistical fluctuations in the electron stream. *Sponsors:* Dr. A. W. Hull, Research Laboratory, General Electric Company; Dr. N. H. Williams, University of Michigan; Dr. P. I. Wold, Union College.

DOCTOR ABRAHAM WHITE, Yale Medical School, $100. *Project:* Study of the proteolysis of proteins. *Sponsors:* Prof. Arthur H. Smith, Yale University; Dr. H. B. Vickery, Connecticut Agricultural Experiment Station; Prof. H. B. Lewis, University of Michigan.

The applications for Sigma Xi grants-in-aid this year numbered twenty-one. Grants were voted to all applicants whose projects are within the fields of research included in the purpose of Sigma Xi. One of the applicants whose research was in the field of chemistry informed the Committee just before its meeting that the grant asked for would not be needed owing to change of plan for the college year, and two whose work is laid in the field of psychology were assisted by a member of the Committee of Award in obtaining grants from other organizations.

WILLIS R. WHITNEY,
HARLOW SHAPLEY,
GARY N. CALKINS.

THE THIRTY-SIXTH CONVENTION

The thirty-sixth Annual Convention of the Society will be held in St. Louis Tuesday, December 31. The executive officers will meet at two o'clock in the afternoon of that day for the second meeting of 1935. The business session will convene at four o'clock, and the fourteenth annual lecture under the auspices of the A. A. A. S. and Sigma Xi will be given in the evening by Mr. John Bellamy Taylor of the Research Laboratory of the General Electric Company.

No one knows better than the National Officers of the Society that it may be difficult for chapters and clubs to send delegates both to the Annual Convention at St. Louis and to the Semi-centennial at Ithaca. Both events are of great importance. It is earnestly hoped that all chapters and clubs will be represented at Ithaca by a large delegation. There can be only one Semi-centennial in the history of the Society, and the arrangements for that important event present such a brilliant program that all who are present are bound to receive profound impressions about the Society and its purpose—namely, the promotion of research.

On the other hand, business of considerable importance is to be presented to the Convention. There will be a number of formal printed petitions for charters, upon which the Convention will be asked by the Executive Committee to take action. Copies of these petitions will be distributed to the chapters well in advance of the Convention in order that chapters may have ample time to acquaint themselves with the scientific conditions at the institutions involved. Officers of the Society are to be chosen for the ensuing biennium, as well as members of the Executive Committee and the Alumni Committee for the succeeding five-year period.

The nominating committee appointed by President Parker to present candidates for these offices is as follows: Prof. Joseph K. Roberts, University of Virginia, Chairman; Prof. B. F. Kingsbury of Cornell University; and Prof. Walter L. Upson of Washington University. Chapters may make suggestions direct to the members of the committee, or through the office of the National Secretary. Alll suggestions will be given careful study by the committee.

It is therefore hoped that chapters and clubs will make an effort to send delegates to the St. Louis meeting. Chapters are entitled to a delegation of not more than three members. Clubs are entitled to one delegate who has the privilege of the floor. In case chapters or clubs are unable to send its own members, they may appoint members of any other chapter as representatives.

CHAPTER OFFICERS

List Furnished by the Secretaries of the Chapters

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EDWARD ELLERY,
National Secretary, Sigma Xi,
Union College,
Schenectady, N. Y.